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# EXCRETION OF MERCURY AFTER CLINICAL INTRAMUSCULAR AND INTRAVENOUS INJECTIONS

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When mercury is administered to a patient, a part generally remains unabsorbed, at least for a time; that which is absorbed circulates through the blood, lymph and tissues, and is then either excreted or deposited and stored in the tissues. This stored mercury may remain in the body for indefinite periods without producing any perceptible toxic or therapeutic effects, for soon after the active absorption of the drug has stopped, but while comparatively large quantities of mercury are not being excreted, the toxic phenomena disappear and the therapeutic effects decline, so that another course of administration must be started to maintain the antisyphilitic action. It may be suggested that the stored mercury has already combined with the tissue proteins, perhaps in insoluble form, so that it does not react further and is therefore really inactive. However this may be, it seems that the actively circulating mercury is chiefly, if not solely, responsible for the effects. The concentration of the circulating mercury determines the amount

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This paper furnished the basis of the Mellon Lecture, Dec. 5, 1930, at Pittsburgh.

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of mercury excreted, especially in the urine; so that, conversely, the amount of urinary mercury should be a fair index of the concentration of active mercury. This is at least a plausible working hypothesis, which emphasizes the importance of the excretion of mercury as a promising approach to the study of mercury therapy. However, the combination in which mercury circulates may also be concerned in its effects, since the reactivity of mercury even in the test tube differs widely according to whether the mercury is in a more or less ionizable form. This is probably unimportant in comparing different doses of the same preparation, but it may be the major determining factor if different compounds are compared, especially when these reach the

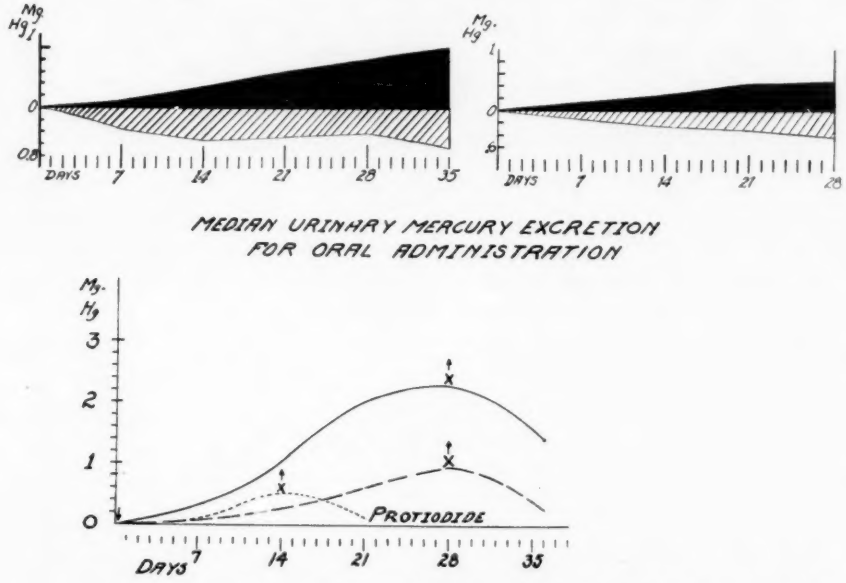


Fig. 1.—The excretion of mercury after inunction and oral administration. In the upper charts the solid portions above the line represent the median urinary excretion of mercury, and the shaded portions below the line represent the median fecal excretion of mercury following simple inunction with 50 and 25 per cent ointments. In the lower chart the heavy line represents the median urinary excretion of mercury for the daily oral administration of 0.5 Gm. of mercury with chalk; the broken line represents the median urinary excretion of mercury for the daily administration of 0.2 Gm. of mercury with chalk, and the dotted line represents the median urinary excretion of mercury for the daily oral administration of 0.016 Gm. of protiodide. The arrow pointing downward indicates the beginning of the treatment, and the arrows pointing upward indicate the end of the treatment. Each division on the left-hand scale represents 0.2 mg. of mercury. All the curves are on the same scale.

blood stream unchanged, as is the case when the drug is injected intravenously and sometimes when it is injected intramuscularly. The present series of studies on excretion illustrates these facts.

As a background to this work, it may be stated that in a series of studies with mercurial inunctions,[1] it was found that the median level of excretion for mercury, both urinary and fecal, is closely proportional to the concentration of mercury in the ointment (fig. 1), i. e., to the dosage of the mercury. In these charts, the urinary mercury is plotted in solid black above the base line, and the fecal mercury as the shaded area below the base line. With the daily inunctions of 4 Gm. of 50 per cent ointment, the excretion rose gradually, so that at the end of the fourth week the median level of daily excretion was 0.83 mg. for the urine and 0.45 mg. for the feces. The maximal excretion attained in a day in any patient was 3.0 mg. for the urine, and 1.3 mg. for the feces. Other authors [2] have reported a similar course with a somewhat higher average for the urine, namely, from 2 to 3 mg. at the end of the fourth week, or practically the maximum figure in our studies. This may be attributed to a more vigorous rubbing by their professional rubbers, especially since our figures on the fecal excretion are somewhat higher than those shown in Lomholt's chart.

Our studies on excretion after oral administration have been completed (but not published) for the three most important preparations, namely, mercury with chalk in daily doses of 0.2 Gm. (77 mg. of mercury) and 0.5 Gm. (192.5 mg. of mercury), mercurous iodide in tablets of ¼ grain (0.016 Gm.) four times a day (39.2 mg. of mercury) and mercuric chloride in 5 mg. tablets three times a day (11.1 mg. of mercury). The 0.2 Gm. dose of mercury with chalk gives a median curve for excretion (fig. 1.) practically identical with the curve for the 50 per cent inunction. The excretion in the after-period is not as enduring with the mercury with chalk, but it is quite considerable. The excretion with the 0.5 Gm. dose of mercury with chalk is more than twice as high as that with the 0.2 Gm. dose, indicating that the absorption of the mercury is approximately parallel to the dosage. The absorption of mercurous iodide appears to be twice as good as that of the mercury with chalk, since it gives the same level of excretion with half of the dose of mercury. For mercuric chloride the excretion was from about one fourth to one third of that for the protiodide, which corresponds closely to the difference in dosage.

With therapeutically effective inunction and oral administration, therefore, the level of urinary excretion in our series is of the order of magnitude of from 0.5 to 2 mg. of mercury at the end of the two or

1. Cole, H. N.; Schreiber, N. E., and Sollmann, T.: Mercurial Ointments in the Treatment of Syphilis, Arch. Dermat. & Syph. **21**:372 (March) 1930.

2. (*a*) Lomholt, S.: Die Zirkulation des Quecksilbers im Organismus, Arch. f. Dermat. u. Syph. **126**:1, 1919. (*b*) Buergi, E.: Grösse und Verlauf der Quecksilberausscheidung durch die Nieren bei den verschiedenen üblichen Kuren, ibid. **79**:3, 1906.

four weeks of administration which are generally considered necessary for therapeutic efficiency.

The studies which follow deal in more detail with intramuscular and intravenous injections of mercuric preparations of several distinct chemical types. In each case the excretion is plotted on the charts in three ways: (1) the daily excretion, (2) the hourly excretion, the time from the moment of injection being plotted logarithmically to save space, and (3) the cumulative excretion, that is, the total quantity of mercury excreted from the beginning of the treatment, obtained by plotting for each day the sum total of urinary mercury or fecal mercury excreted up to that time. The cumulative fecal excretion of mercury is plotted above the cumulative urinary mercury, thus giving the total cumulative excretion for any day. The total quantity of mercury injected is shown by the step-line superimposed on the others. The quantity retained corresponds to the distance between this and the curve for excretion.

In order to make the charts for the various injections directly comparable, they have been reproduced on the same scale. When the figure for excretion was too low to be plainly visible on the ordinary scale, it was multiplied by ten, as indicated in the legend. The injections are shown on the charts by downward arrows. The charts also show the effects on the output of urine, which is generally increased by mercurial medication, but this may form the subject of another communication.

The numerical results are generally reported as the "total range," and the "median." The total cumulative excretion for sixteen weeks after the last injection was obtained by free-hand graphic extrapolation, i. e., by free-hand projection of the curve for excretion. Before the end of the sixteen weeks this curve becomes essentially horizontal in practically all the cases, so that it need not be projected further.

The general time scheme for the collection of the excreta was as follows: After a fore-period of two days which established the absence of mercury, the injection was given at about 1 p. m., and specimens of urine were collected at intervals of one, two, four, eight, sixteen, twenty-four and forty-two hours after the injection, then daily from 7:00 a. m. to 7:00 a. m. on the following day, until the next injection. The feces were collected daily or as obtainable, but with many patients the fecal data appear to be incomplete.

The method used for the determination of mercury was the micrometric method described by Schreiber, Sollmann and Booth.[3]

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3. Schreiber, N. E.; Sollmann, T., and Booth, H. S.: The Determination of Traces of Mercury, J. Am. Chem. Soc. **50**:1620 (June) 1928.

MERCURIC SODIUM BROMIDE BY INTRAMUSCULAR INJECTIONS

Mercuric sodium bromide (fig. 2) was administered in place of the widely used sodium mercuric iodide because the iodine would complicate the analytic method. The absorption should be the same. The double bromide contains the mercury in relatively highly ionized form, especially since the sodium bromide probably diffuses more rapidly than the mercuric bromide, which then combines with the proteins in the tissues to form the less ionized compounds. It was administered exclusively by intramuscular injection as a solution of mercuric bromide and sodium bromide, 4 Gm. of each in 100 cc. of water. The dose, 0.25 cc., contained 10 mg. of mercuric bromide, equivalent to 5.5 mg. of mercury. A series of daily injections, continued through a period of from two to four weeks, was reported in a previous article.[4] In the present series of three patients the injections were spaced somewhat differently, so as to be comparable with those of the other compounds: The first, second and third injections were made at intervals of a week; but since the excretion of mercury was very low, the third injection was followed by daily injections. However, considerable stomatitis developed in one of the patients soon after the first daily injection, and in two patients after the second daily injection, notwithstanding the low level of the excretion of mercury. As the stomatitis increased in severity the daily injections were spaced at longer and somewhat irregular intervals. The dentition of all the patients was good. It may be added that in the first series salivation occurred with unusual frequency, i. e., in 66 per cent of the patients, as contrasted with 39 per cent for the simple inunctions.

*Daily Excretion of Mercury.*—After the first injection the urinary excretion remained low for the entire week, ranging between 0.01 and 0.10 mg. per day, with half of the values between 0.01 and 0.035 mg. In the week following the second injection it rose but little higher, half of the values ranging between 0.03 and 0.05 mg. with a maximum of 0.22 mg. The fecal excretion was of the same order of magnitude. Even after the daily injections were started, the excretion rose but little in patient D. C. L., somewhat more in patient W. S., in whom the urinary mercury ranged between 0.49 and 0.55 mg. after the third daily injection and the third day after the fifth daily injection; it fell to 0.37 mg. two days later, and with the next injection rose to 0.61 mg. The fecal excretion was somewhat lower; in W. S. it reached a maximum of

4. Cole, H. N.; Gammel, J. A.; Rauschkolb, J. E.; Schreiber, N. E., and Sollmann, T.: Clinical Excretion of Mercury: After Intramuscular Injections of Mercuric Bromide, After Simple, and After Clean Inunction, Arch. Dermat. & Syph. **17**:625 (May) 1928.

EXPLANATION OF FIGURES 2 TO 8

The solid blocks above the line indicate the urinary excretion, and the shaded portions below the line, the fecal excretion. The arrows pointing downward indicate the day of injection, and the figures above the arrows give the dosage administered. The dotted lines indicate the volume of urine. Each division on the left-hand scale represents 0.2 mg. of mercury, and 50 cc. of urine. For amounts too small to reproduce, the chart has been enlarged by the multiple indicated. The daily intervals between the injections are marked on the lower part of the chart.

In the charts for hourly excretion of mercury, the time has been plotted logarithmically. The dotted lines indicate the hourly excretion of urine. Each division on the scale represents 0.2 mg. of mercury and 20 cc. of urine.

In the charts which represent the cumulative excretion of mercury, the upper solid line indicates the total amount of mercury administered; the dotted line represents the total amount of mercury excreted in the urine and feces, and the lower solid line indicates the amount of mercury excreted in the urine. Each division on the scale represents 2.5 mg. of mercury. The interval of days after each injection is marked on the scale on the lower part of the chart.

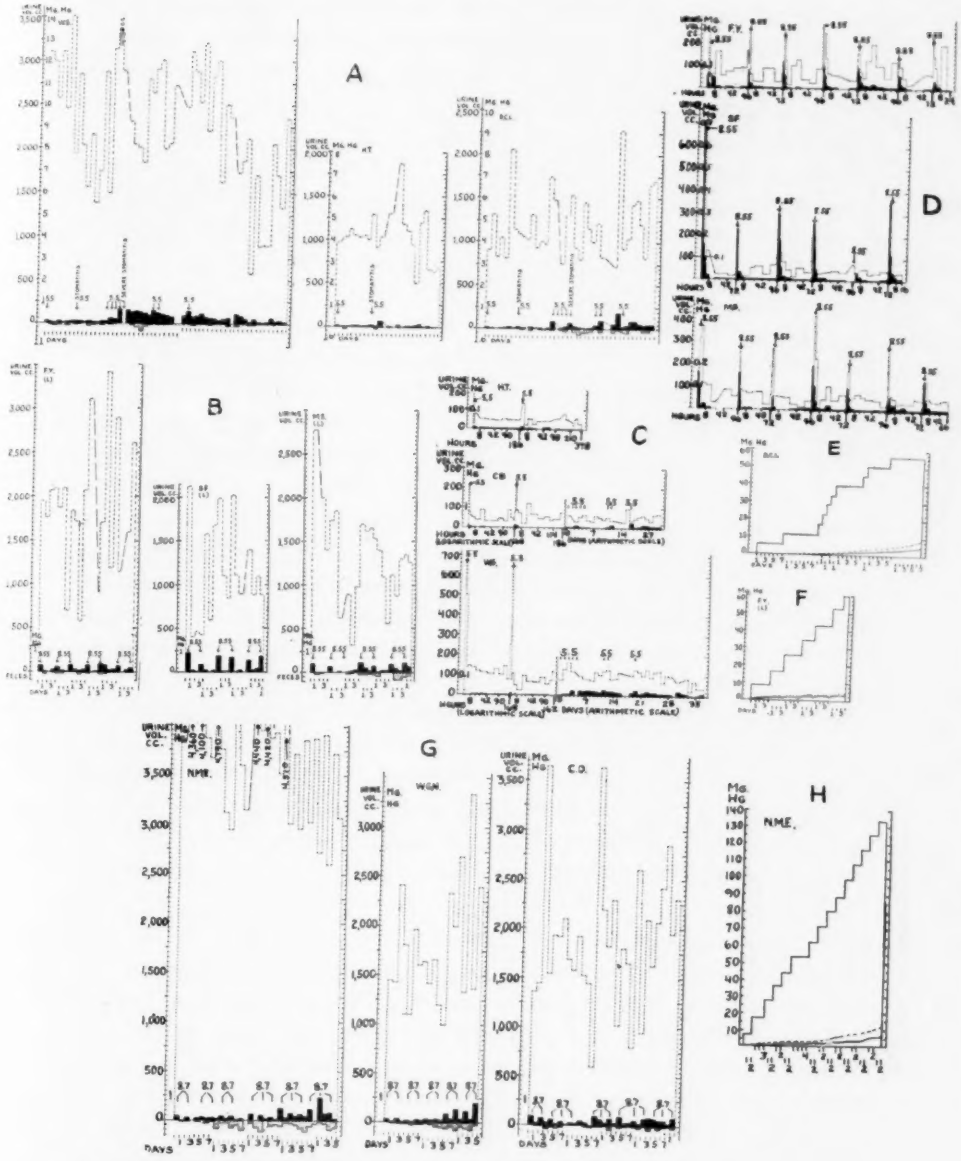



Fig. 2.—*A* indicates the daily excretion of mercury following the intramuscular injection of mercuric sodium bromide; *B*, the daily excretion following the intravenous injection of mercuric oxycyanide; *C*, the hourly excretion following the intramuscular injection of mercuric sodium bromide; *D*, the hourly excretion following the intravenous injection of mercuric oxycyanide; *E*, the cumulative excretion following the intramuscular injection of mercuric sodium bromide; *F*, the cumulative excretion following the intravenous injection of mercuric oxycyanide; *G*, the daily excretion, and *H*, the cumulative excretion following the intramuscular injection of mercuric benzoate.

0.33 mg.; in D. C. L. it ranged between 0.04 and 0.26 mg. per day. With the continued daily injections extending over periods of from two to four weeks, as reported in the article cited, the excretion rose more rapidly, the daily urinary excretion reaching the median of 0.38 mg. at the end of the first week, 0.45 mg. at the end of the second week and 0.98 mg. at the end of the fourth week. The corresponding figures for the fecal excretion were 0.08, 0.25 and 0.3 mg. at the end of the first, second and fourth weeks. In the earlier series the median ratios of urinary to fecal mercury at the end of these weeks were 4:1, 3:1 and 23:1.

In two patients receiving daily injections of mercuric chloride, who were studied by Buergi,[2b] the urinary excretion followed a similar course, but the level was from 2.5 to 3.1 mg. of mercury at the end of four weeks, about three times as high as in our studies. The daily dosage of the mercury, however, was also higher, equivalent to 7.4 mg. of mercury, and large doses of potassium iodide were administered at the same time.

*Hourly Urinary Excretion of Mercury.*—With weekly injections the excretion reached its greatest intensity in one or two hours after the injection and declined somewhat by the fourth hour. The maximal rate, however, was quite low, namely, between 0.01 and 0.02 mg. per hour. It appears, therefore, that a small quantity of the mercury was absorbed directly but that the larger part was fixed almost immediately in the tissues and absorbed very slowly, so that by the next day and on the succeeding days, the urinary excretion ranged between 0.001 and 0.0025 mg. per hour. With daily injections, which gave a larger number of foci of absorption, the hourly level of excretion was maintained slightly higher, about 0.015 mg., with a maximum of 0.028 mg.

*Cumulative Excretion and Retention of Mercury.*—The chart shows that a type patient, D. C. L., who received nine injections (49.5 mg. of mercury) had excreted a total of 3.76 mg. of mercury after the four week course: 2.14 mg. in the urine and 1.62 mg. in the feces. During the period of thirty-nine days, in which 55.5 mg. of mercury was injected, only about one seventh of the injected mercury had been excreted, six sevenths remaining in the body indefinitely. Approximately the same ratio was obtained in the former series, notwithstanding the difference in dosage. In Buergi's patients who received mercuric chloride the total excretion at the end of the five weeks was reported to be much higher, namely, from 35 to 48 per cent; about one fifth of the excreted mercury was in the feces. We have no data as to how much of the unexcreted mercury is unabsorbed and how much may have been retained in the organs.

MERCURIC OXYCYANIDE BY INTRAVENOUS INJECTION

The intravenous injection of mercuric chloride was introduced by Baccelli, and by Tommasoli,[5] a 1 per cent solution of mercuric chloride in 3 per cent solution of sodium chloride being injected in a dose of 1 cc., or 10 mg. of mercuric chloride, every day or on alternate days, thirty doses constituting a course. The clinical results were at best no better than with other methods, but obliterating phlebitis was often produced. Intravenous injections of other preparations of mercury caused less local damage, but the therapeutic results were rather indifferent, so that the treatment with intravenous injections of mercury has been practically abandoned.

In order to avoid phlebitis, we employed the much less irritant mercuric oxycyanide, $Hg(CN)_2HgO$, which is often used as a substitute for mercuric chloride (fig. 2). It is a basic salt of hydrocyanic acid, containing from 51.7 to 56 per cent of mercuric cyanide and from 44.3 to 48 per cent of mercuric oxide, a total of 85.5 per cent of mercury. It was administered by intravenous injection twice a week, in doses of 5 cc. of a 0.2 per cent solution, containing 10 mg. of mercuric oxycyanide (8.55 mg. of mercury).

The urinary excretion of mercury was found to be of the same type as for the intravenous injections of the other soluble mercuric preparations, novasurol and salyrgan (which will be discussed later), except for the level obtained, which more closely resembled that obtained with the intramuscular injections of sodium mercuric bromide. There was no case of salivation.

*Daily Urinary Excretion of Mercury.*—With this series of injections there was a marked initial excretion of mercury during the first twenty-four hours after each injection. For the first injection it was 0.32 mg. for F. Y., 0.40 mg. for M. S., and 1 mg. for S. F. This level of excretion, however, did not increase for the successive injections. From the twenty-fourth to the forty-second hour after each injection there was a drop in the amount of mercury excreted. After the first injection the level of excretion fell to 0.02 mg. for F. Y. and to 0.04 mg. for S. F. With the later injections the fall was not quite so marked; from the twenty-fourth to the forty-second hour following the fourth injection the level was 0.15 mg. for F. Y., 0.08 mg. for M. S. and 0.02 mg. for S. F. By the second and third day after each injection the excretion of mercury had fallen very low, in some cases to zero.

*Hourly Urinary Excretion of Mercury.*—The excretion of mercury reached its highest level in one or two hours after each injection and then dropped rapidly, so that by the sixteenth hour it was almost

5. Tommasoli: Le traitement intense et précoce de la syphilis par les injections intravéineuses de sublimé, Ann. de dermat. et syph. **3**:1073, 1903.

negligible. The maximum excretion of 0.69 mg. in the case of S. F., was obtained one hour after the first injection. The median hourly excretion of mercury was as follows: up to one hour, 0.12 mg. (from 0.02 to 0.69 mg.); from one to two hours, 0.06 mg. (from 0 to 0.18 mg.); from two to four hours, 0.03 mg. (from 0 to 0.06 mg.); from four to eight hours, 0.015 mg. (from 0.005 to 0.03 mg.); from eight to sixteen hours, 0.005 mg. (from 0.002 to 0.01 mg.); from sixteen to twenty-four hours, 0.003 mg. (from 0 to 0.02 mg.).

*Fecal Excretion of Mercury.*—The data for the fecal excretion of mercury are meager. In the case of M. S. it varied from 0.02 to 0.33 mg. and appeared to increase gradually with the number of injections, reaching a maximum of 0.33 mg. on the two days following the sixth injection; but there was no marked increase on the day of the injection. In the case of F. Y. the excretion varied from 0.02 to 0.11 mg., also showing no marked increase on the day of the injection.

*Cumulative Excretion and Retention of Mercury.*—The chart shows a type patient, F. Y. After seven injections (59.85 mg. of mercury) over a period of twenty-two days, a total of 4.05 mg. of mercury was excreted, 3.12 mg. in the urine and 0.93 mg. in the feces. This is about 6.7 per cent or one fifteenth of the total amount injected. Over a period of sixteen weeks this amounted to about 4.75 mg. or about 8 per cent of the total amount injected.

### MERCURIC BENZOATE BY INTRAMUSCULAR INJECTIONS

Mercuric benzoate $(C_6H_5COO)Hg.H_2O$ is the mercuric salt of benzoic acid and is often administered in preference to mercuric chloride. It contains about 43.5 per cent of mercury, and for intramuscular injections is usually administered in doses of 1 cc. of a 2 per cent solution with 2.5 per cent solution of sodium chloride, every second day. It is thought that a part of the mercury is thus in the form of the bichloride. Lomholt [6] found no untoward symptoms when small amounts were injected, but doses of from 100 to 200 mg. caused pain and a marked rise in temperature, so that the patient was often confined to bed. He injected 100 mg. of mercuric benzoate (43.5 mg. of mercury) once a week, but we administered only 20 mg. of mercuric benzoate (8.7 mg. of mercury) every other day, so that our results are not comparable. We found no untoward symptoms in any of the three patients, and the clinical results were also negative.

*Daily Urinary Excretion of Mercury.*—Figure 2 shows that the daily excretion was low. During the first twenty-four hours after the injection it ranged between 0.07 and 1.05 mg. with a median of 0.22

6. Lomholt, S.: Investigations into the Circulation of Some Heavy Metals in the Organism (Hg, Bi, and Pb), Biochem. J. **18**:691, 1924; footnote 2a.

mg., and during the period from the twenty-fourth to the forty-second hour it fell to about one fourth of this level: from 0 to 0.24 mg. with a median of 0.05 mg. The maximum excretion of 1.05 mg. (N. M. E.) was obtained during the first twenty-four hours after the fourteenth injection, and 0.82 mg. (W. G. N.) after the tenth injection. With intramuscular injections of 100 mg. of mercuric benzoate, Lomholt found a maximum urinary excretion of 5.4 mg. on the day of the second injection and in another patient an excretion of 9.24 mg. of mercury on the day of the sixth injection.

*Hourly Urinary Excretion of Mercury.*—This was almost too low to be of any significance, but it appeared to be highest during the first two hours and then declined gradually to a negligible value. The median excretion on the day of the injection was as follows: up to one hour, 0.03 mg. (from 0 to 0.08 mg.); from one to two hours, 0.03 mg. (from 0 to 0.10 mg.); from two to four hours, 0.02 mg. (from 0 to 0.10 mg.); from four to eight hours, 0.01 mg. (from 0 to 0.05 mg.); from eight to sixteen hours, 0.005 mg. (from 0 to 0.01 mg.); from sixteen to twenty-four hours, 0.005 mg. (from 0 to 0.07 mg.).

*Fecal Excretion of Mercury.*—The fecal excretion of mercury was slightly higher than the urinary excretion. In the case of N. M. E. and W. G. N. it was low at the beginning of the treatment and gradually increased with the number of injections but appeared to have no relation to the day of injection. In the case of C. O. it varied considerably and was usually higher on the day of the injection. For C. O. it varied from 0 to 0.18 mg.; for N. M. E., from 0 to 0.45 mg., and for W. G. N., from 0 to 0.30 mg.

*Cumulative Excretion and Retention of Mercury.*—At the end of twenty-eight days a type patient, N. M. E., had received thirteen injections (113.1 mg. of mercury). The urinary excretion of mercury was 3.86 mg. and the fecal, 5.70 mg., making a total of 9.56 mg. or about 8.5 per cent of the amount injected. Over a period of sixteen weeks the total excreted amounted to about 11 mg. or 10 per cent of the quantity injected.

### BICHLORIDOL BY INTRAMUSCULAR INJECTIONS

Bichloridol was a preparation of mercuric chloride suspended in a fatty base (fig. 3). It was injected intramuscularly, twice a week, from gelatin capsules, containing, according to the manufacturers, 1 grain (0.065 Gm.) of corrosive mercuric chloride (60 mg. $HgCl_2$ = 44.34 mg. Hg). However, it has been found that the gelatin of the capsules gradually abstracts the mercury, so that the mercury content changes and can only be known by actual analysis. (The preparation has been withdrawn from the market.) At the end of the injections the capsules were found to contain only 4.84 mg. of mercury. At the time of the injections the amount was presumably higher, especially in the earlier

injections. The actual dosage could not even be guessed, but it was of course at least 4.8 mg. of mercury per injection. The excretion was less than with an equivalent dosage of the aqueous mercuric sodium bromide, and there was no therapeutic effect, so that a serologic relapse set in under the treatment. No salivation occurred in any of the patients. There was, however, some diuretic response to half of the injections.

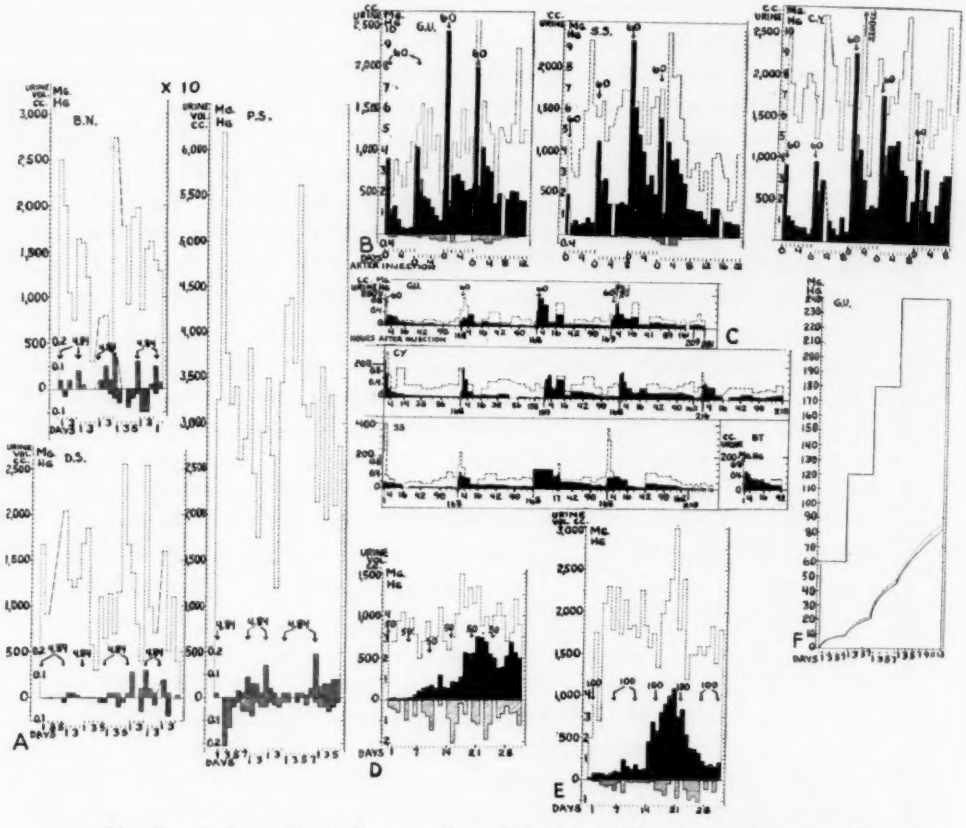



Fig. 3.—*A* shows the daily excretion of mercury following the intramuscular injection of bichloridol; *B*, the daily excretion of mercury following a single weekly intramuscular injection of mercuric salicylate; *C*, the hourly excretion of mercury following the intramuscular injection of mercuric salicylate; *D*, the daily excretion of mercury following the intramuscular injection of mild mercurous chloride (Lomholt); *E*, the daily excretion following the intramuscular injection of mercuric oil (Lomholt); *F*, the cumulative excretion following the intramuscular injection of mercuric salicylate.

*Daily Urinary Excretion of Mercury.*—The excretion of mercury was low throughout the treatment but was highest on the day of the injection. The medians of the first twenty-four hours after the injec-

tions were as follows: 0.02 mg. for D. S., 0.14 mg. for P. S., and 0.10 mg. for B. N. From the twenty-fourth to the forty-second hour after the injection the level fell to a median of 0.02 mg. for D. S., of 0.03 mg. for B. N., and of 0.04 mg. for P. S. The following days the excretion of mercury was negligible, usually zero. The highest excretion throughout the series was 0.20 mg. (P. S.) during the first twenty-four hours after the injection.

*Fecal Excretion of Mercury.*—The fecal excretion of mercury was also low: from 0 to 0.08 mg., with a median of 0.02 mg., for D. S.; from 0 to 0.10 mg., with a median of 0.02 mg., for B. N., and from 0 to 0.21 mg., with a median of 0.04 mg., for P. S.

*Cumulative Excretion and Retention of Mercury.*—The cumulative excretion was small for the three patients. D. S., who received seven injections in thirty-one days, excreted a total of 0.90 mg. of mercury; B. N., who received six injections in twenty-three days, excreted a total of 1.36 mg. of mercury, and P. S., who received five injections in twenty-eight days, excreted a total of 2.21 mg. of mercury.

### COMPARISON OF THE MODE OF ADMINISTRATION OF IONIZABLE MERCURIC COMPOUNDS: SODIUM BROMIDE, OXYCYANIDE, BENZOATE AND CORROSIVE CHLORIDE

These compounds are sufficiently similar in dosage and in the form of mercury to be comparable, so that the data obtained with them show the relation of the excretion to the method of administration. It may be recalled that the mercuric oxycyanide was administered intravenously twice a week in doses of 10 mg., or 8.55 mg. of mercury; the bichloridol (in oil) was given intramuscularly twice a week in doses of at least 4.84 mg. of mercury; the mercuric sodium bromide (in water) was administered intramuscularly at varying intervals in doses of 10 mg., or 5.5 mg. of mercury and the mercuric benzoate was given intramuscularly, in doses of 20 mg., or 8.7 mg. of mercury every other day.

*Daily Urinary Excretion of Mercury.*—With all three methods, this was highest on the day of the injection, but the levels were markedly different. With the intravenous administration of mercuric oxycyanide, the excretion on the day of the injection ranged between 0.19 and 0.97 mg. with a median of 0.39 mg. of mercury, and this did not increase with succeeding injections. With the intramuscular injection of mercuric sodium bromide, bichloridol and mercuric benzoate the levels were very low after the first injections, the medians being 0.05 mg., 0.02 mg. and 0.18 mg. of mercury. The levels rose, however, on continued injections, presumably by multiplication of the depots resulting from the injections. With mercuric sodium bromide, the median of

0.45 mg. was attained after nine injections; with the bichloridol, the rise was much less, namely, to the median of 0.16 mg. after the fifth injection. With the mercuric benzoate the median of 0.50 mg. was attained after the tenth injection.

The higher excretion occurring with intravenous administration of mercuric oxycyanide was of short duration, and on the day after the injection the level was not much higher than that following intramuscular injections, the fall from the medians of the first day to the second day being as follows: For mercuric oxycyanide, from 0.39 mg. to 0.07 mg.; for mercuric sodium bromide, from 0.10 mg. to 0.05 mg.; for mercuric benzoate, from 0.08 mg. to 0.05 mg., and for bichloridol, from 0.05 mg. to 0.02 mg.

*Hourly Urinary Excretion of Mercury.*—During the administration of the aforementioned compounds the hourly excretion of mercury was too low to be accurately measured.

*Cumulative Urinary Excretion of Mercury.*—For a twenty-eight day course of treatment the cumulative excretion compares as follows for the type patients:

| Preparation | Mg. of Mercury Administered | Mg. of Mercury Recovered | Percentage Recovered |
|---|---|---|---|
| Mercuric oxycyanide, 22 days..... | 59.85 | 3.12 | 5.2 |
| Mercuric sodium bromide, 28 days.... | 49.50 | 2.14 | 4.3 |
| Mercuric benzoate, 28 days..... | 113.10 | 3.86 | 3.4 |
| Bichloridol, 28 days..... | ..... | 0.85 | .. |

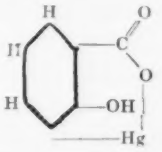
*Recapitulation.*—The excretions of these four compounds have similar orders of magnitude, but that with the intravenous injection of mercuric oxycyanide was highest and that with the intramuscular injection of oily base bichloridol was lowest. The difference was most marked following the early injections and on the first day of each injection. With the intravenous injections a prompt excretion of the mercury is secured, but the level is not maintained. Intramuscular injections of aqueous solutions must be repeated several times to establish multiple depots before a satisfactory level of excretion is reached; but once it is reached, it persists between injections. Injections of oily preparations give less excretion for a given dosage then do watery solutions, probably owing to slower absorption from the intramuscular depots.

### MERCURIC SALICYLATE BY INTRAMUSCULAR INJECTIONS

The excretion of mercuric salicylate (fig. 3) has been described in a previous article,[7] but may be briefly reviewed to correlate it with the

7. Cole, H. N.; Gammel, J. A.; Schreiber, N. E., and Sollmann, T.: Mercuric Salicylate. A Study of Its Excretion in the Treatment of Syphilis, Arch. Dermat. & Syph. **19**:105 (Jan.) 1929.

other compounds. According to Dimroth,[8] it is an anhydride of ortho-oxymercuri-salicylic acid:




The direct union of one mercury valence to the carbon ring makes the compound firmer, so that it is ionized but very little and does not precipitate protein but is dissolved by the latter and causes moderate pain. It was administered by weekly intramuscular injections of 100 mg. of the mercuric salicylate, equivalent to 60 mg. of mercury, suspended in vegetable oil.

*Daily Excretion of Mercury.*—Quantitatively this presents a picture very different from that of the watery solutions of the ionizable compounds such as mercuric sodium bromide. The urinary excretion of mercury during the first twenty-four hours after the injections ranged between 1.9 and 9.66 mg. of mercury, the quantity increasing progressively with repeated injections up to the third injection. From the twenty-fourth to the forty-second hour the level had fallen to half or less, ranging between 0.78 and 6.10 mg. of mercury; then it continued to fall gradually, ranging between 0.3 and 2.16 mg. of mercury at the end of the week. These figures are quite similar to those of Buergi,[2b] and of Lomholt.[2a] It may also be mentioned that the quantity of urine was generally increased with each injection. The fecal excretion did not show the acute increase with each injection and was much smaller than the urinary excretion, ranging between 0.02 and 0.46 mg. per day. Salivation did not occur in any of the patients, but a severe diarrhea developed in one patient, S. S.

*Hourly Urinary Excretion of Mercury.*—As illustrated in the chart on a type patient, G. U., the maximal rate of excretion of mercury occurred in from two to four hours, ranging between 0.13 and 0.87 mg. per hour; it then declined gradually, but rather rapidly, to about 0.04 to 0.38 mg., with a median of 0.1 mg. per hour, by the end of twenty-four hours, and to about 0.01 to 0.08 mg., with a median of 0.06 mg., by the end of the week.

*Cumulative Excretion and Retention of Mercury.*—The chart shows marked retention. During the four weeks' course in which a type patient, G. U., received four injections (240 mg. of mercury), a total of 74.5 mg. of mercury was excreted, 68.5 mg. in the urine and about

8. Dimroth, O.: Ueber die Mercurirung aromatischer Verbindungen, Ber. d. deutsch. chem. Gesellsch. **35**:2853, 1902.

6 mg. in the feces; thus about two thirds of the amount administered was retained. Extrapolation of the curve indicates that four months after the injection about 140 mg. of the total 240 mg. of mercury injected would have been excreted. At that time the rate of excretion would have fallen so low that the remainder would stay in the body almost indefinitely. In Buergi's and Lomholt's patients the retention was even somewhat greater; in Buergi's two patients the urinary excretion was 34.9 and 27.3 per cent of the amount injected; in Lomholt's two patients the urinary plus the fecal excretion of mercury was 38.6 and 49.4 per cent.

### WATER-INSOLUBLE MERCURIC PREPARATIONS SUSPENDED IN OIL

Intramuscular injections of oily suspensions of finely divided mild mercurous chloride and of mercuric oil (fig. 3) furnish depots from which the mercury is absorbed only as it is converted into soluble compounds. Since this is a slow process, an injection continues to supply mercury for a considerable time, so that treatments can be spaced at weekly intervals. The same property, however, leads to uncontrollable cumulation and to capricious effects, and these have resulted in serious and sometimes fatal mercurial poisoning. The injections of mild mercurous chloride have the further drawback of being very painful. These injections of insoluble preparations have, therefore, been practically abandoned in this country, and we did not feel justified in reviving them, especially as the data gathered in earlier days by other observers suffice to define the character of their excretion. The charts are drawn from these data.

For mercuric oil, Lomholt [6] analyzed the excretion of a patient who received the equivalent of 100 mg. of mercury, every five days, for six injections. The following tabulation shows the daily level for excretion of mercury at the end of each week:

| | Urine, Mg. of Mercury | Feces, Mg. of Mercury |
|---|---|---|
| First week | 0.40 | 0.52 |
| Second week | 0.94 | 0.11 |
| Third week | 4.38 | 1.00 |
| Fourth week | 0.89 | 0.50 |

These figures illustrate the circulation of effective quantities of mercury, but they also illustrate the dangerous variations, the urinary level rising in the third week to five times the level for the second and fourth week. It should also be noted that the levels for excretion generally ascend progressively with the injections. The total excretion amounted to 9.6 per cent of the quantity injected.

For mild mercurous chloride in oil, data for one patient are given by Buergi [2b] and for two patients by Lomholt.[6] The latter injected 50 mg.

of mild mercurous chloride every five days, for five or six injections. The chart shows that the excretion increased gradually to about 2.25 mg. of mercury per day in the urine after the fourth week, and to about 0.5 mg. in the feces; the total excretion was 21.5 per cent of the amount injected. Buergi used double the dosage and obtained higher levels for

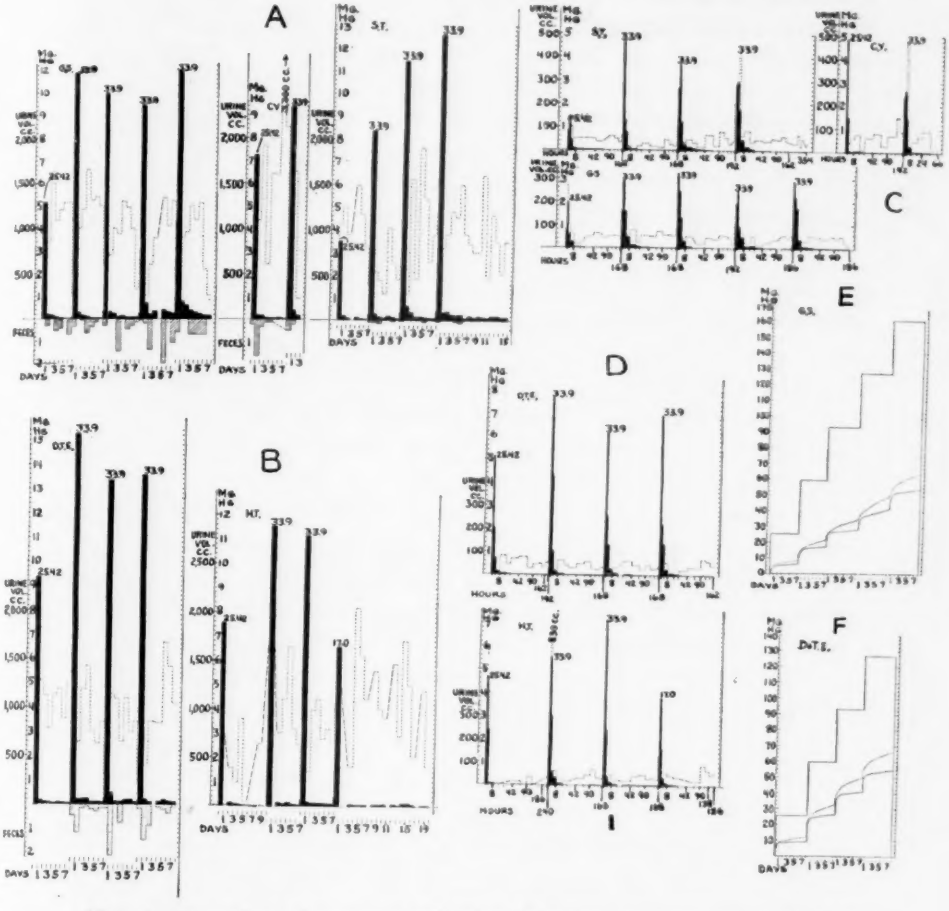


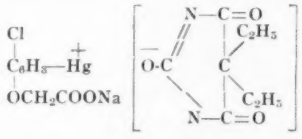

Fig. 4.—Excretion of mercury following injections of novasurol: A, daily excretion following intramuscular injection; *B*, daily excretion following intravenous injection; *C*, hourly excretion following intramuscular injection; *D*, hourly excretion following intravenous injection; *E*, cumulative excretion following intramuscular injection; *F*, cumulative excretion following intravenous injection.

urinary excretion: from 5 to 7 mg. on the day of injection, falling gradually to about 2 or 3 mg. on the third day. The total urinary excretion of mercury in thirty-nine days was 31 per cent of the amount injected, considerably more than for the mercuric oil.

The chief characteristic of the excretion of the "insoluble" preparations is that the quantity does not increase on the day of the injection, but rises slowly in the intervals to levels which tend to exceed those of the inunctions and of the ionizable injections and which are subject to unexplained spontaneous variations. In fact, these variations may reach such a height as to be dangerous to the patient, and, of course, they are uncontrollable.

### NOVASUROL INTRAMUSCULAR INJECTIONS

Novasurol is a complex compound with the probable formula:



The mercury is very firmly bound, with little or no ionization. The preparation is administered intramuscularly or intravenously. The clinical efficiency against syphilis is said to be positive, but low and unsuited to energetic treatment. However, it is quite liable to produce minor toxic effects, especially diarrhea. These may be due to the molecule, rather than to the mercury ions.

Novasurol was administered intramuscularly once a week from the commercial ampules. The first injection in each patient was 0.75 cc., containing 10 per cent novasurol, equivalent to 25.42 mg. of mercury. The subsequent injections were each of 1 cc., equivalent to 33.9 mg. of mercury. Neither salivation nor diarrhea occurred in any of the three patients.

*Daily Excretion of Mercury.*—The urinary excretion of mercury during the first twenty-four hours after the first injection of 25.42 mg. of mercury ranged between 3.45 and 7.25 mg., with a median of 5.16 mg. With the later injections of 33.9 mg., as described in a previous article,[9] the entire range was between 8.33 and 12.60 mg., with a median of 10.56 mg. In one patient the excretion appeared to increase markedly with each successive injection, but in another there was no increase. From the twenty-fourth to the forty-second hour after the injection of 33.9 mg. of mercury, the urinary excretion of mercury fell to the level of from 0.18 to 0.58 mg., with a median of 0.27 mg., that is, about one fortieth of the level for the first twenty-four hours. By the end of each week, it ranged between 0.03 and 0.24 mg. The volume of urine appeared to attain its peak toward the middle of the

9. Sollmann, T.; Cole, H. N.; Schreiber, N. E.; Rauschkolb, J. E., and Gammel, J. A.: The Clinical Excretion of Mercury, Am. J. Physiol. **90**:523 (Oct.) 1929.

week, i. e., several days after the injection. The fecal excretion also reached its maximum several days after injection, and this maximum, which ranged between 1.02 and 1.95 mg., was universally higher than for the salicylate.

*Hourly Urinary Excretion of Mercury.*—The chart emphasizes the acuteness of the excretion. The maximum was reached within the first hour after the injection; for the doses of 33.9 mg. it ranged as follows: up to one hour, 2.75 mg. (from 1.64 to 4.68 mg.); from one to two hours, 2.55 mg. (from 1.32 to 3.70 mg.); from two to four hours, 1.36 mg. (from 0.79 to 1.74 mg.); from four to eight hours, 0.36 mg. (from 0.09 to 0.47 mg.); from eight to sixteen hours, 0.08 mg. (from 0.03 to 0.14 mg.); from sixteen to twenty-four hours, 0.05 mg. (from 0.02 to 0.10 mg.). It is clear, therefore, that the circulating mercury leaves the blood and tissues promptly.

*Cumulative Excretion and Retention of Mercury.*—Notwithstanding the acuteness of the excretion, about two thirds of the injected mercury was not excreted within a week. Of the total of 127.12 mg. of mercury injected during the four weeks into a type patient, G. S., a total of 57.5 mg. was excreted: 40.2 mg. in the urine and 17.3 mg. in the feces. Of the total of 161 mg. injected during thirty-six days, a total of 74.7 mg. was excreted: 53.6 mg. in the urine and 21.1 mg. in the feces. The total excretion, sixteen weeks after the completion of the course, estimated by free-hand projection of the curve for excretion, would be about 84 mg.—so that about half of the injected mercury remains indefinitely in the body. Judging from the prompt initial excretion, and from the similar retention after intravenous injection, it appears that this mercury must be bound after its absorption. Its distribution among different organs would form an interesting topic for future investigation.

### NOVASUROL BY INTRAVENOUS INJECTIONS

Intravenous injections were given with the same dosage and intervals as the intramuscular injections (fig. 4). The excretion is of the same type as with the intramuscular injections, except that the immediate urinary excretion of mercury is even more intense, and this also raises the total excretion of mercury. However, the persistent retention is still about half of the quantity injected. It is evident, therefore, that the retention is not due to failure of absorption but to actual fixation in the tissues.

The volume of urine increased to about the same extent as with intramuscular injections, but with intravenous administration the volume generally reached its maximum on the day of the injection, showed a compensatory decline on the following day, then a rise up to the third

or fourth day and a more gradual decline later on. The fecal excretion is about the same as with intramuscular injections. It is remarkable that two of the three patients, H. T. and S. K., reacted with severe diarrhea, while the intramuscular injections did not produce this result. (The observations on S. K. are not included in the figure.) None of the patients showed any salivation.

*Daily Excretion of Mercury.*—The urinary excretion was definitely higher than for the intramuscular injections. For the dose of 25.4 mg., the urinary excretion for the first twenty-four hours was 7.6 and 9.3 mg.; for the dose of 33.9 mg. the range was between 6.56 and 15.25 mg., with a median of 12.34 mg. From the twenty-fourth to the forty-second hour the urinary excretion had fallen to the level of from 0.12 to 0.18 mg., with a median of 0.14 mg., and at the end of the week it was from 0.04 to 0.10 mg., with a median of 0.08 mg. The fecal excretion increased acutely with each injection from 0.05 mg. to a maximum of 2.10 mg.; by the end of the week it had fallen to the level of from 0.14 to 0.11 mg.

*Hourly Urinary Excretion of Mercury.*—The chart shows even more strikingly the acuteness of the urinary excretion of mercury. With the doses of 33.9 mg. the medians were as follows: up to one hour, 6.55 mg. (from 3.78 to 7.70 mg.); from one to two hours, 2.48 mg. (from 1.53 to 4.28 mg.); from two to four hours, 0.82 mg. (from 0.32 to 1.36 mg.); from four to eight hours, 0.22 mg. (from 0.08 to 0.34 mg.); from eight to sixteen hours, 0.06 mg. (from 0.02 to 0.07 mg.); from sixteen to twenty-four hours, 0.02 mg. (from 0.01 to 0.03 mg.).

*Cumulative Excretion and Retention of Mercury.*—In a type patient, D. T. E., about half of the mercury was retained, notwithstanding the rapid rate of excretion. During the course of administration of twenty-eight days in which 127 mg. of mercury was injected, the total excretion amounted to 67 mg. of mercury: 54.9 mg. in the urine and 12.1 mg. in the feces. This is about 53 per cent of the amount of mercury injected. Sixteen weeks after the termination of the course, the total excretion was estimated at about 80 mg. or about 63 per cent of the amount injected, so that about one third was retained indefinitely.

### SALYRGAN BY INTRAMUSCULAR INJECTIONS

Salyrgan was introduced as a diuretic. It has been used to some extent in Germany as an antisyphilitic preparation, although recognized to be of only moderate worth. Linser[10] has employed it as well as

10. Linser, P., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 18, p. 591.

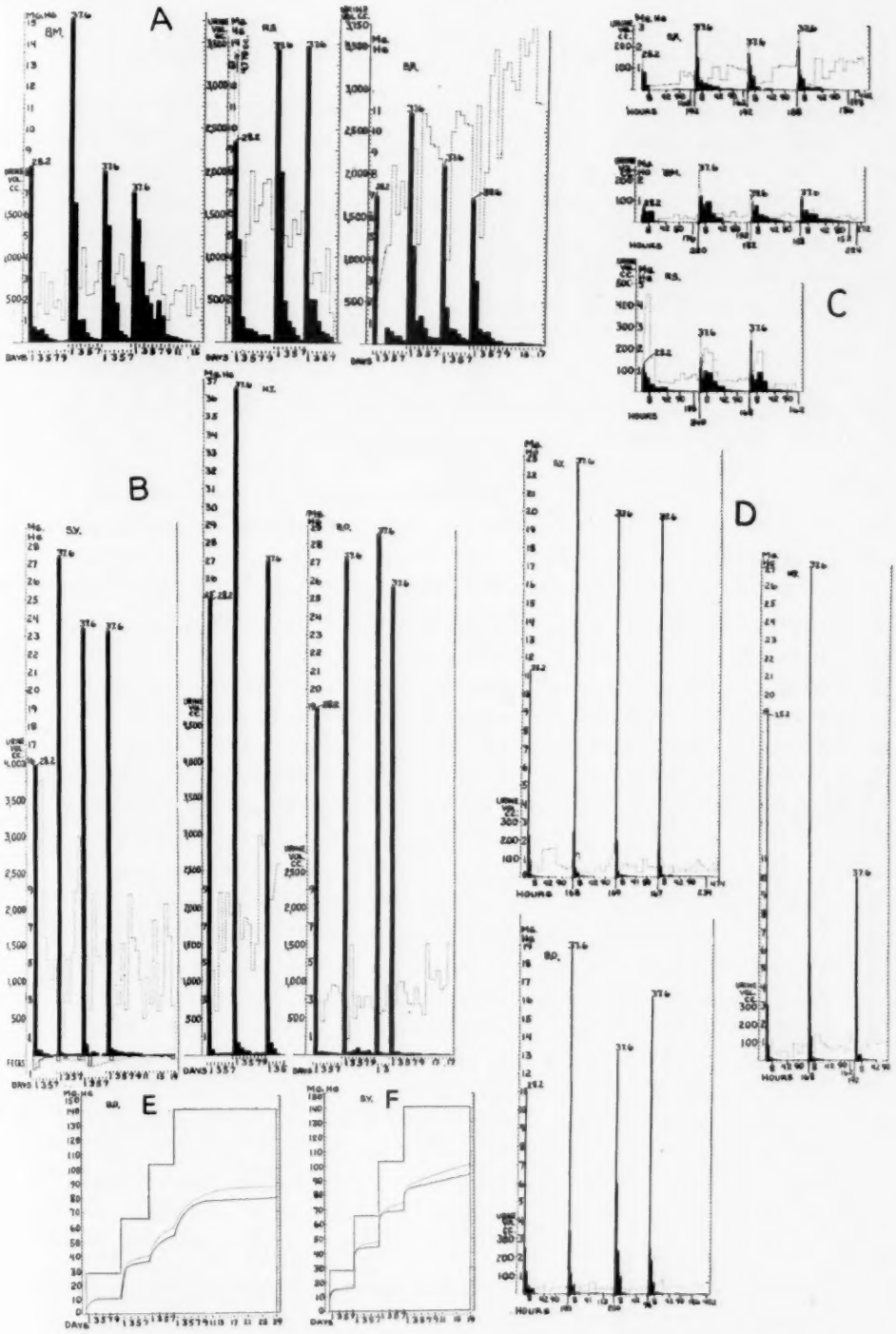
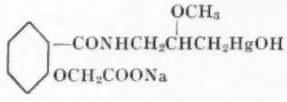



Fig. 5.—Excretion of mercury following injections of salyrgan: *A*, daily excretion following intramuscular injection; *B*, daily excretion following intravenous injection; *C*, hourly excretion following intramuscular injection; *D*, hourly excretion following intravenous injection; *E*, cumulative excretion following intramuscular injection; *F*, cumulative excretion following intravenous injection.

mercuric chloride, novasurol and other preparations for his so-called mixture preparation for administering neoarsphenamine. A 10 per cent solution of salyrgan is added to a 10 per cent solution of the arsenical compound and administered intravenously. Linser and others claim excellent clinical results without any bad effects from this mixed technic.

The composition of salyrgan is given as:




According to this, the mercury, not being directly united to the benzene ring, should be more easily ionized than in novasurol; and it was found that about 10 per cent of the mercury in neutral solution of salyrgan is precipitated by hydrogen sulphide in ten minutes. Nevertheless, it appears less liable to produce diarrhea than novasurol, perhaps because it is excreted more rapidly.

Salyrgan was administered similarly to the novasurol, namely, at weekly intervals, with a first injection of 0.75 cc., equivalent to 28.2 mg. of mercury and subsequent injections of 1 cc., equivalent to 37.6 mg. of mercury. The intensity of the immediate excretion approaches that for novasurol administered intramuscularly; but the excretion declines more slowly, as seen in the daily, and especially in the hourly curve. This prolonged excretion is due purely to slower absorption, for it will be shown that it does not occur with intravenous injections. The total cumulative excretion is somewhat higher than with novasurol, but of the same order of magnitude. The fecal excretion was not well studied. The urinary excretion is variable, but on the whole it appears higher than with novasurol. Neither salivation nor diarrhea occurred.

*Daily Urinary Excretion of Mercury.*—During the first twenty-four hours after the first injection of 28.2 mg. of mercury the urinary excretion of mercury ranged between 8.36 and 10.50 mg. With the later injections of 37.6 mg., the daily excretion was as follows: up to twenty-four hours, 9.95 mg. (from 7.38 to 17.24 mg.); from twenty-four to forty-two hours, 2.90 mg. (from 1.02 to 4.40 mg.), and at the end of the week, 0.19 mg. (from 0.08 to 0.26 mg.). The excretion from the twenty-fourth to the forty-second hour was about one fourth of that of the first day; then it descended gradually in a parabolic curve. Successive injections produced about the same rate of excretion.

*Hourly Urinary Excretion of Mercury.*—After injections of 37.6 mg. of mercury, the hourly excretion of mercury was as follows: up to one hour, 0.25 mg. (from 0.11 to 0.89 mg.); from one to two hours, 1.68 mg. (from 0.19 to 2.76 mg.); from two to four hours, 0.72 mg. (from 0.43 to 1.48 mg.); from four to eight hours, 0.58 mg. (from

0.43 to 0.93 mg.); from eight to sixteen hours, 0.37 mg. (from 0.13 to 0.93 mg.); from sixteen to twenty-four hours, 0.30 mg. (from 0.08 to 0.45 mg.).

*Cumulative Excretion and Retention of Mercury.*—The chart shows a type patient, B. O., who received four injections, totaling 141 mg. of mercury. During the twenty-eight days of the course of treatment 87.5 mg. of mercury was excreted: 72.1 mg. in the urine and 15.4 mg. in the feces. This is about 62 per cent of the amount of mercury injected. After sixteen weeks the cumulative excretion was about 97 mg. of mercury or about 68.8 per cent of the total amount injected. Thus, about one third of the injected mercury was retained, although at times the excretion was enormous and rapid.

*Inefficiency of Salyrgan Against Syphilis.*—Notwithstanding the high level of excretion of mercury and the large amount retained in the tissues after intramuscular injections of salyrgan, no therapeutic response was observed in the three patients with acute syphilis on whom it was tried. Therefore, the mercury is not in an active form, either in the blood or in the tissues. The essential data are as follows:

CASE 1.—A man, who had a primary lesion on the genitalia and who gave positive results on dark field examination, received 0.75 cc. of salyrgan intramuscularly on March 21, 1930. Results of dark field examination were positive on March 22 and 23, negative on March 24 and 25 and positive again on March 26.

CASE 2.—A patient with condylomata lata in whom dark field examination gave positive results, received 0.75 cc. of salyrgan intramuscularly. The medication did not bring about a disappearance of the organisms.

CASE 3.—A woman with extensive macular papular syphilitic lesions was given 0.75 cc. of salyrgan intramuscularly, and the dose was repeated in three days. There was no Herxheimer reaction, and the eruption became more intense.

### SALYRGAN BY INTRAVENOUS INJECTIONS

Intravenous injections of salyrgan were given at weekly intervals, in the same dosage as the intramuscular injections (fig. 5). The urinary excretion of the mercury rose promptly to very high figures, the output on the first day being two or three times as high as for the intramuscular administration of salyrgan or intravenous injections of novasurol. This high level of excretion was confined especially to the first hour, when it was from two to four times as high as for the intravenous administration of novasurol and about ten times as high as for intramuscular injections of salyrgan. The cumulative excretion was also distinctly higher than for any of the other drugs and methods studied, but, nevertheless, about one third of the mercury was retained indefinitely. In contrast to the reaction to the intravenous administration of novasurol, none of the patients showed either salivation or diarrhea. The diuretic response was also distinctly higher than with the other

drugs or methods, and it usually reached its maximum on the day of the injection. This was followed by a compensatory fall on the second or third day, and then by a rise.

*Daily Urinary Excretion of Mercury.*—On the first day after the injection of 28.2 mg. of mercury the amount excreted ranged between 15.85 and 24.98 mg., with a median of 18.97 mg. of mercury. With later injections of 37.6 mg., the excretion was as follows: up to twenty-four hours, 27.2 mg. (from 23.24 to 36.89 mg.); from twenty-four to forty-two hours, 0.24 mg. (from 0.12 to 0.52 mg.), and at the end of the week, 0.09 mg. (from 0.06 to 0.12 mg.).

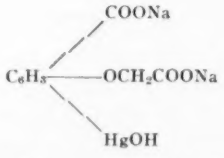
*Hourly Urinary Excretion of Mercury.*—After injections of 37.6 mg. of mercury, the excretion of mercury was as follows: up to one hour, 14.7 mg. (from 1.46 to 27.20 mg.); from one to two hours, 5.7 mg. (from 1.98 to 22.60 mg.); from two to four hours, 1.2 mg. (from 0.31 to 2.41 mg.); from four to eight hours, 0.3 mg. (from 0.09 to 0.51 mg.); from eight to sixteen hours, 0.06 mg. (from 0.03 to 0.08 mg.); from sixteen to twenty-four hours, 0.03 mg. (from 0.01 to 0.08 mg.).

*Fecal Excretion of Mercury.*—The data on the fecal excretion of mercury are rather incomplete, but on a type patient, S. Y., it varied from 0.03 to 0.74 mg. No marked increase appeared on the day of the injection.

*Cumulative Excretion and Retention of Mercury.*—The chart shows a type patient, S. Y., who received four injections, totaling 141 mg. of mercury. After the four weeks' course of treatment, the cumulative excretion of mercury was 97.1 mg.: 93.9 mg. in the urine and 3.2 mg. in the feces. This is about 68.8 per cent of the amount injected. In sixteen weeks the cumulative excretion was about 112 mg. of mercury or about 80 per cent of the total amount injected.

### MERCUROSAL BY INTRAMUSCULAR INJECTIONS

Mercurosal (fig. 6) is an organic preparation of mercury having the formula:




and containing from 43 to 43.8 per cent of mercury in organic combination. It is administered either intramuscularly or intravenously. The usual intramuscular dose is 0.05 Gm. (21.7 mg. of mercury) dissolved in 2 cc. of sterile water, every fourth or fifth day for from ten to twelve doses. No untoward symptoms appeared in the patients whose excre-

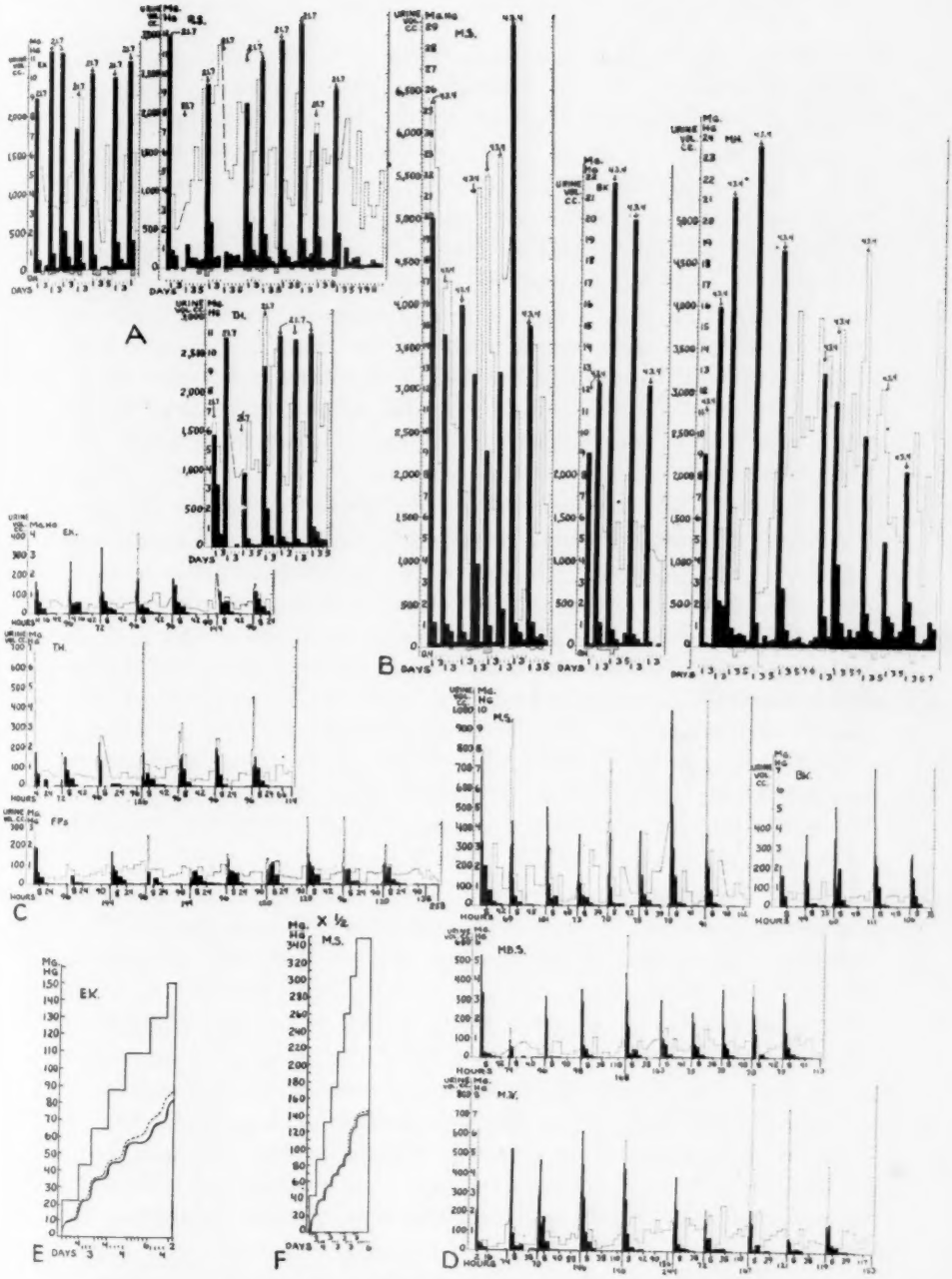



Fig. 6.—Excretion of mercury following injections of mercurosal: *A*, daily excretion following intramuscular injection; *B*, daily excretion following intravenous injection; *C*, hourly excretion following intramuscular injection; *D*, hourly excretion following intravenous injection; *E*, cumulative excretion following intramuscular injection; *F*, cumulative excretion following intravenous injection.

tion charts are reproduced. In one patient, M. Y., bloody diarrhea developed after the second injection, and the medication was discontinued. (The observations on M. Y. are not included in the figure.)

*Daily Urinary Excretion of Mercury.*—This resembled the excretion of mercury after intramuscular injections of novasurol or salyrgan. Up to the twenty-fourth hour after the injection of 21.7 mg. of mercury the urinary excretion of mercury ranged from 7.88 to 12.80 mg., with a median of 11.10 mg.; from the twenty-fourth to the forty-second hour it ranged from 0.19 to 1.02 mg. of mercury, with a median of 0.48 mg., which is about one twentieth of the amount excreted during first twenty-four hours. By the fourth day after the injection the level of excretion fell to from 0.10 to 1.01 mg., with a median of 0.28 mg. of mercury. There appeared to be no gradual increase with progressive injections, but usually there was a rise after two or three injections and then a decline, followed by another gradual increase.

*Hourly Urinary Excretion of Mercury.*—The chart illustrates the rapidity of the excretion. The maximum was usually reached in from one to four hours after the injection; it then declined rather rapidly and at the end of twenty-four hours was almost negligible. The medians and range are as follows: up to one hour, 0.90 mg. (from 0.33 to 1.90 mg.); from one to two hours, 1.56 mg. (from 0.12 to 3.28 mg.); from two to four hours, 1.01 mg. (from 0.23 to 1.83 mg.); from four to eight hours, 0.68 mg. (from 0.30 to 1.11 mg.); from eight to sixteen hours, 0.33 mg. (from 0.06 to 0.61 mg.); from sixteen to twenty-four hours, 0.09 mg. (from 0.01 to 0.22 mg.); from twenty-four to forty-two hours, 0.03 mg. (from 0.01 to 0.08 mg.).

*Fecal Excretion of Mercury.*—This was uniformly low in comparison with the urinary excretion of mercury, ranging between 0.04 and 0.30 mg. of mercury. There was a slight noticeable increase on the day after the injection.

*Cumulative Excretion and Retention of Mercury.*—The chart shows a type patient, E. K., who received 151.9 mg. of mercury in twenty-seven days. During this time 82.04 mg. of mercury was excreted in the urine and about 5.25 mg. in the feces, making a total of 87.3 mg., or 57.4 per cent of the amount injected. Over a period of sixteen weeks this amounted to about 91 mg. of mercury, or about 60 per cent of the amount injected. Thus about one third is indefinitely retained in the body.

### MERCUROSAL BY INTRAVENOUS INJECTIONS

From ten to twelve doses of 0.1 Gm. of mercurosal (43.3 mg. of mercury), dissolved in 5 cc. of sterile water, were injected intravenously, a dose every second or third day (fig. 6). The excretion of mercury was of the same type as with intramuscular injections, except that it was

higher and more rapid and resembled the excretion with intravenous injections of novasurol. The dose was twice that of the intramuscular injection, and it was administered twice as often. Untoward symptoms appeared in two cases: In one patient, M. Y., bloody diarrhea developed after the second injection and the medication was discontinued. The other patient, M. B. S., who received 0.1 Gm. at the first injection, was not able to tolerate this dose owing to bloody diarrhea and was given only 0.05 Gm. at each succeeding injection.

*Daily Urinary Excretion of Mercury.*—There appeared to be a gradual increase in the excretion of mercury up to the third injection; then there was a decrease, followed by another gradual increase as the number of injections increased. The daily urinary excretion of mercury was a little more intense than with the intramuscular injections: Up to twenty-four hours, 14.46 mg. (from 5.94 to 29.66 mg.) was excreted; from the twenty-fourth to the forty-second hour, 0.52 mg. (from 0.11 to 2.70 mg.); on the third day after the injection, 0.46 mg. (from 0.10 to 1.92 mg.).

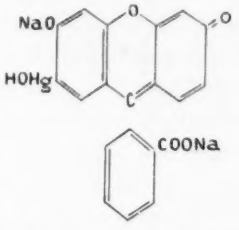
*Hourly Urinary Excretion of Mercury.*—The chart shows the rapidity of the excretion of mercury during the first and second hours and the sharp decline. The hourly excretion was as follows: up to one hour, 2.86 mg. (from 0.69 to 9.90 mg.); from one to two hours, 3.30 mg. (from 0.72 to 5.17 mg.); from two to four hours, 1.46 mg. (from 0.23 to 5.22 mg.); from four to eight hours, 0.59 mg. (from 0.14 to 1.92 mg.); from eight to sixteen hours, 0.18 mg. (from 0.02 to 0.48 mg.); from sixteen to twenty-four hours, 0.07 mg. (from 0.02 to 0.27 mg.).

*Fecal Excretion of Mercury.*—In the three patients, M. N., M. S. and B. K., the excretion was low (from 0 to 0.9 mg.) with no marked increase on the day of the injection. M. B. S., who could not tolerate the usual intravenous dose, showed a high fecal excretion of mercury during the first two weeks (from 0.18 to 2.52 mg.), but during the remainder of the treatment, when only half of the dose was administered, the excretion was also low (from 0.08 to 0.45 mg. of mercury).

*Cumulative Excretion and Retention of Mercury.*—A type patient, M. S., received eight injections of 43.3 mg. of mercury each, making a total of 346.4 mg. Over a period of twenty-eight days the urinary excretion was 142.43 mg. of mercury, and the fecal excretion of mercury was 3.37 mg., making a total of 145.8 mg., which is about 42 per cent of the total amount injected. Over a period of sixteen weeks this amounted to about 150 mg. of mercury, or about 45 per cent of the total amount injected. Thus from about three fifths to one half was retained.

FLUMERIN BY INTRAVENOUS INJECTIONS

Flumerin (fig. 7) is the disodium salt of 2-hydroxy-mercurifluorescein, with the formula:




It contains theoretically 33.83 per cent of mercury; 32.5 per cent was found by analysis. According to White, Hill, Moore and Young,[11] doses of 3 mg. per kilogram of body weight given intravenously on alternate days are clinically antisyphilitic. Our studies on excretion comprised four patients who received intravenously at each injection 10 cc. of a 2 per cent aqueous solution, equivalent to 200 mg. of flumerin, or 65 mg. of mercury, corresponding to the ordinary therapeutic dose. Four injections were given to each patient at weekly intervals except that for one patient, H. S., two weeks intervened between the first and the second injection because of malarial reactions. Another patient, E. E., was diabetic; this, however, did not appear to alter the response to mercury. The urinary excretion of mercury was intermediate between that for the soluble and that for the colloidal mercury preparations administered intravenously. It started promptly and reached its maximum in the second hour at a level which was fairly high but much lower than that for equal quantities of mercury in the soluble organic compounds, novasurol and salyrgan. On the other hand the excretion continued at a moderate level for some days after the injection, indicating that the mercury is deposited in the blood stream in a mobilizable form, similar to the deposition with colloidal preparations, such as mercuric sulphide or the metal. The fecal excretion of mercury was higher than with any other mercury compound studied, indicating that the mercury may be excreted by the liver into the bile.

*Daily Urinary Excretion of Mercury.*—This was always highest during the first twenty-four hours after the injection, ranging between 0.96 and 6.14 mg. with a median of 2.26 mg. of mercury. From the twenty-fourth to the forty-second hour it fell to about one sixth: from 0.10 to 0.90 mg. with a median of 0.35 mg. of mercury. It continued to fall, reaching from 0.10 to 0.56 mg., with a median of 0.25 mg. by

11. White, E. C.; Hill, J. H.; Moore, J. E., and Young, H. H.: Flumerin—A New Mercurial for the Intravenous Treatment of Syphilis, J. A. M. A **79**:877 (Sept. 9) 1922.

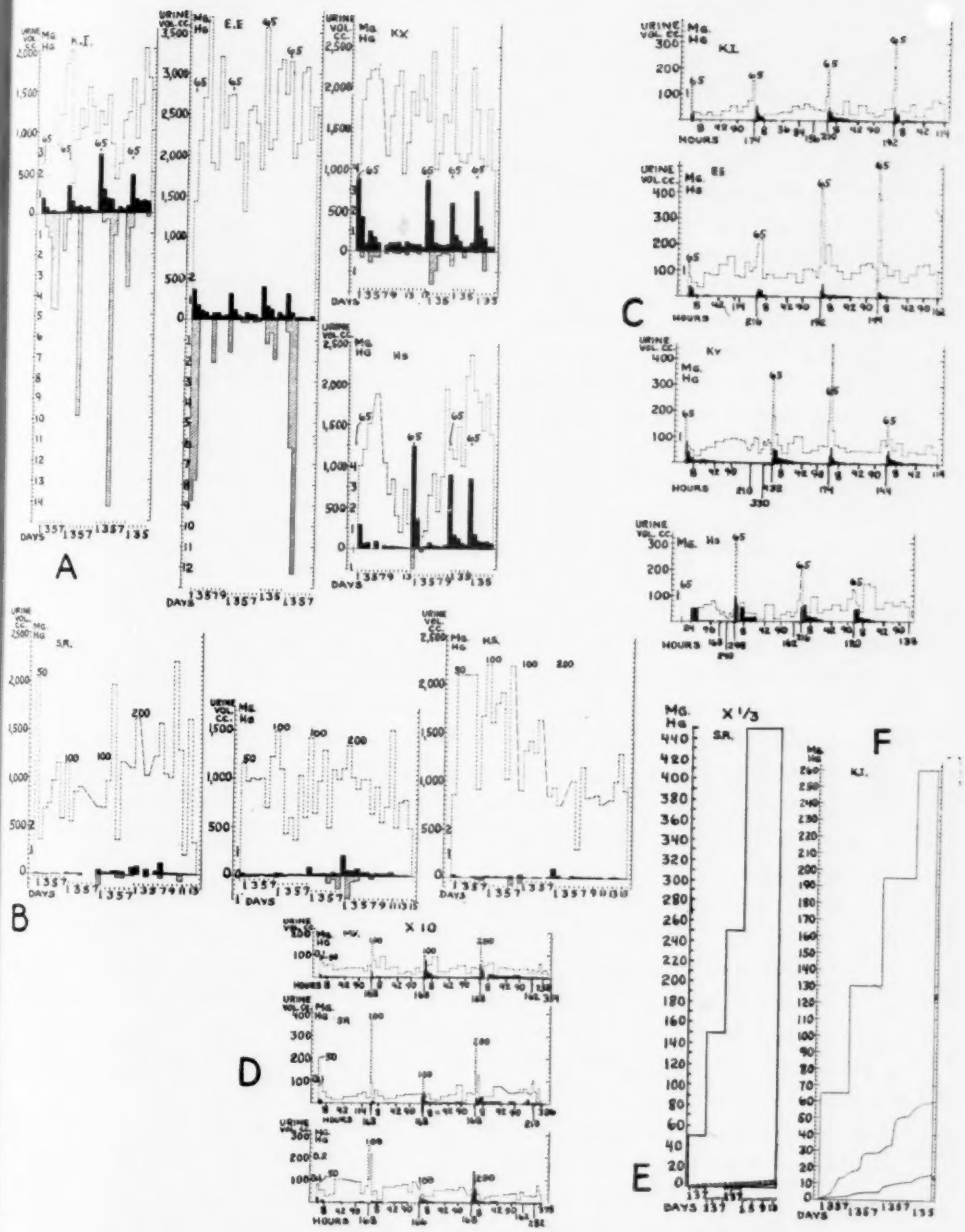



Fig. 7.—*A* indicates the daily excretion of mercury following the intravenous injection of flumerin; *B*, the daily excretion following the intravenous injection of colloidal metallic mercury; *C*, the hourly excretion following the intravenous injection of flumerin; *D*, the hourly excretion following the intravenous injection of colloidal metallic mercury; *E*, the cumulative injection following the intravenous injection of colloidal metallic mercury; *F*, the cumulative excretion following the intravenous injection of flumerin.

the end of the week. The variations for repeated injections did not show any definite trend.

*Hourly Urinary Excretion of Mercury.*—This was relatively high during the first hour but did not generally reach its maximum until the second hour, indicating that the excretion occurred more slowly than with novasurol or salyrgan or with the ionized compounds. It also remained rather high during the third hour, as seen from the numerical data: up to one hour, 0.27 mg. (from 0.04 to 0.94 mg.); from one to two hours, 0.45 mg. (from 0.20 to 0.76 mg.); from two to four hours, 0.23 mg. (from 0.09 to 0.48 mg.); from four to eight hours, 0.10 mg. (from 0.02 to 0.17 mg.); from eight to sixteen hours, 0.06 mg. (from 0.01 to 0.15 mg.); from sixteen to twenty-four hours, 0.04 mg. (from 0.02 to 0.15 mg.).

*Fecal Excretion of Mercury.*—This was highest on the day of the injection or on the next day, and then declined rather gradually. The maximal excretion for any one day ranged between 0.96 and 14.3 mg., with a median of 6.96 mg. of mercury. The total fecal excretion of mercury during the whole course, including the week after the last injection, ranged from 8.25 to 43.89 mg. with a median of 43.46 mg. The median amounted to about 16.7 per cent of the injected mercury and was to the total urinary mercury excretion as 3.3: 1.

*Cumulative Excretion and Retention of Mercury.*—The chart shows the data for a type patient, K. I., who received four injections of 65 mg. of mercury each, totaling 260 mg. A week after the last injection the cumulative excretion was 59.5 mg. of mercury: 15.6 mg. in the urine and 43.9 mg. in the feces, which is about 23 per cent of the amount injected. In sixteen weeks the cumulative excretion amounted to about 74 mg., or 31 per cent of the amount injected. Thus about two thirds of the mercury was retained.

*Untoward Symptoms.*—These are known to be rather common with intravenous injections of flumerin; stomatitis or albuminuria is said to develop in about one third of the patients. In the present series, two patients did not show reactions; in two, H. S. and K. Y., soreness of the mouth developed in a few days and K. Y. felt nauseated for two or three hours after each injection. None of the patients showed albuminuria or microscopic evidence of renal damage.

High metallic excretion suggests the possibility of the use of this preparation in infections of the gallbladder and biliary tract.

### COLLOIDAL METALLIC MERCURY BY INTRAVENOUS INJECTIONS

The colloidal metallic mercury (fig. 7) employed is a fine trituration of metallic mercury with five parts of dextrose. The particles of mercury are said to range in size "from the diameter of a blood corpuscle"

to ultramicroscopic dimensions. The powder is suspended in water in the ratio of 0.3 Gm. of the preparation containing 0.05 Gm. of mercury to 5 cc. of water, so that it contains 10 mg. of mercury per cubic centimeter. It is probable that the colloidal particles are caught and retained in the reticulocytes and other cells, or that they conglomerate in the capillaries and thus form depots from which absorption occurs. Cole, Hutton, Rauschkolb and Sollmann [12] found the large doses which were formerly advised therapeutically effective but dangerous. A part of the mercury may therefore be converted into an active form. Rothwell and Maloney [13] also claimed good therapeutic results from smaller doses, but the following observations indicate that the activation is low and uncertain. It is possible that the considerable quantities of mercury which remain in the body are potentially harmful.

In the present series, the colloidal metallic mercury was injected at weekly intervals in the successive doses of 50, 100, 100 and 200 mg. of mercury. The chief characteristic is the very low urinary excretion of mercury, increasing slightly with the number of injections and somewhat more with the size of the dose, but returning promptly to the lower levels. The maximal excretion appeared between two and four hours after the injection. The fecal excretion was about as high as with the other methods. The total cumulative excretion a week after the end of the four week course of injections was about one fourth that for the inunctions with 50 per cent mercury and one sixteenth that for the intravenous administration of salyrgan. There was neither salivation nor diarrhea.

*Daily Urinary Excretion of Mercury*—After the first injection of 50 mg. of colloidal metallic mercury the daily excretion was as follows: up to twenty-four hours, 0.07 mg. (from 0.04 to 0.10 mg.); from twenty-four to forty-two hours, 0.01 mg. (from 0 to 0.02 mg.); at the end of the week, 0.02 mg. (from 0 to 0.02 mg.). This was followed by two injections of 100 mg. of mercury each at weekly intervals, and by a fourth injection of 200 mg. of mercury. After the injection of 200 mg. of mercury, the daily excretion was as follows: up to twenty-four hours, 0.41 mg. (from 0.36 to 0.93 mg); from twenty-four to forty-two hours, 0.14 mg. (from 0.10 to 0.26 mg.); at the end of the week, 0.07 mg. (from 0.05 to 0.09 mg.).

*Hourly Urinary Excretion of Mercury.*—The excretion of mercury was as follows: For injections of 50 mg. of mercury, up to one hour,

12. Cole, H. N.; Hutton, J. G.; Rauschkolb, J. E., and Sollmann, T.: Metallic Mercury Suspensions, J. A. M. A. **83**:593 (Aug. 23) 1924.

13. Rothwell, J. J., and Maloney, E. R.: The Intravenous Use of Metallic Mercury (Mercodel) in the Treatment of Syphilis, Am. J. Syph. **9**:413 (July) 1925.

0.01 mg. (from 0 to 0.02 mg.); from one to two hours, 0.02 mg. (from 0.01 to 0.02 mg.); from two to four hours, 0 mg. (from 0 to 0.02 mg.); from four to eight hours, 0.005 mg. (from 0 to 0.01 mg.); from eight to sixteen hours, 0.0025 mg. (from 0 to 0.0025 mg.); from sixteen to twenty-four hours, 0 mg. (from 0 to 0.001 mg.). For injections of 200 mg. of mercury: from 0 to one hour, 0.04 mg. (from 0.03 to 0.06 mg.); from one to two hours, 0.04 mg. (from 0.02 to 0.14 mg.); from two to four hours, 0.03 mg. (from 0.025 to 0.06 mg.); from four to eight hours, 0.01 mg. (from 0.01 to 0.14 mg.); from eight to sixteen hours, 0.01 mg. (from 0.006 to 0.015); from sixteen to twenty-four hours, 0.01 mg. (from 0.0025 to 0.01 mg.).

*Cumulative Excretion and Retention of Mercury.*—The chart shows data on a type patient, S. R., who received four injections, totaling 450 mg. of mercury. A week after the last injection, the cumulative excretion was 6.3 mg. of mercury: 2.7 mg. in the urine and 3.6 mg. in the feces, or about 1.4 per cent of the total amount injected. In sixteen weeks the cumulative excretion was about 13 mg., or 2.8 per cent of the amount injected. This shows a retention of mercury even higher than for the colloidal mercuric sulphide. The form in which it is retained and whether that form is dangerous are questionable.

### COLLOIDAL MERCURIC SULPHIDE (MERSULFOL) BY INTRAVENOUS INJECTIONS

Mersulfol (fig. 8) is an aqueous colloidal solution of mercuric sulphide, containing about 2 per cent of mercuric sulphide (1 cc. = 17 mg. of mercury). It was administered intravenously in doses of 10 cc. of the 2 per cent solution (170 mg. of mercury), twice a week. Soreness of the mouth occurred in two of the patients after the third injection, necessitating a longer interval before the fourth injection. The chief characteristics of these injections was the rather wide variation of the urinary excretion of mercury in the three patients, the gradual increase after the third injection and the marked increase with each following injection. The level of the urinary excretion of mercury at times rose to 3 mg. per day. Considerable daily fluctuations occurred which were parallel to the amount of urine excreted and appeared to be a reflection of it.

It seems, therefore, that the intravenous injection of mercuric sulphide results in deposits from which effective quantities of mercury may be liberated, as shown by the salivation, by the persistent diuresis and by the high level of excretion. However, the level of excretion varied widely in different patients, and when high levels were established they continued for weeks. This renders it impossible really to control the dosage. The occurrence of salivation in all the patients indicates that this may be dangerous.

*Daily Urinary Excretion of Mercury.*—The urinary excretion of mercury was as follows: up to twenty-four hours, 0.38 mg. (from 0.02 to 2.79 mg.); from twenty-four to forty-two hours, 0.08 mg. (from 0.01 to 3.62 mg.); at the end of the week, 1.15 mg. (from 0.01 to 4.36 mg.).

*Hourly Urinary Excretion of Mercury.*—The hourly excretion after the first and second injections was too small to be significant, but

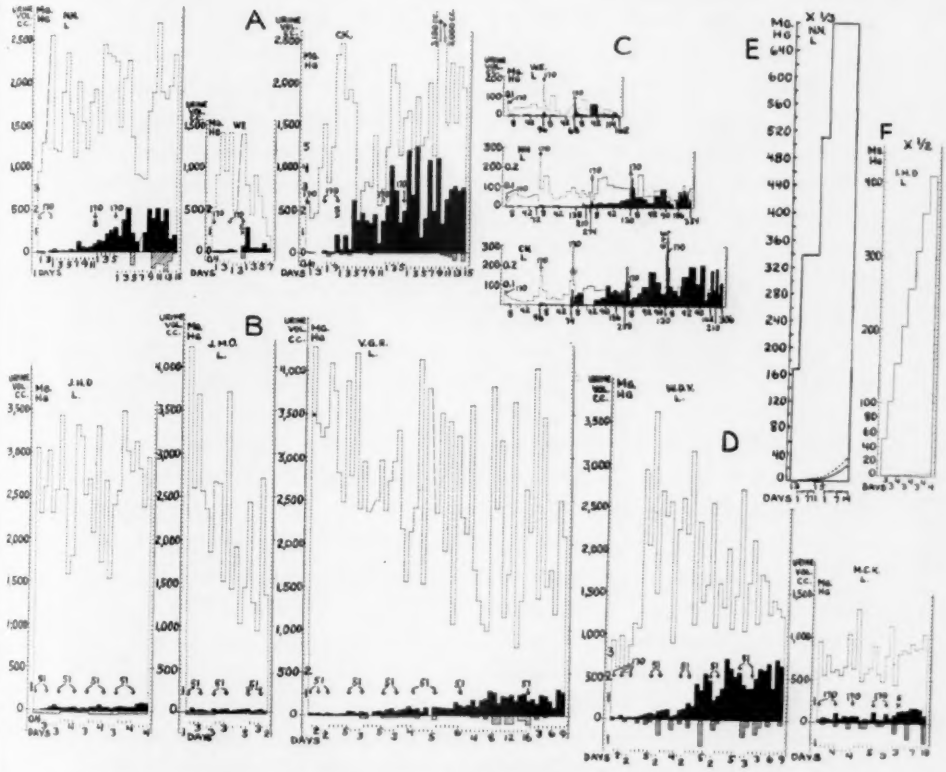



Fig. 8.—Excretion of mercury following injections of mersufol: *A*, daily excretion following intravenous injection; *B*, daily excretion following intramuscular injection; *C*, hourly excretion following intravenous injection; *D*, hourly excretion following intramuscular injection; *E*, cumulative excretion following intravenous injection; *F*, cumulative excretion following intramuscular injection.

after the third injection, when the quantity became larger, it could be noted that it was distinctly higher in the first two hours, namely, 0.04 mg. per hour, after which it continued fairly uniform at 0.02 mg. per hour to the sixteenth hour. After the fourth injection, the concentration of the mercury was sufficiently high to show that the maximum excretion occurred between the first and second hours. The medians

of the hourly excretion after all the injections were as follows: up to one hour, 0.02 mg. (from 0 to 0.45 mg.); from one to two hours, 0.02 mg. (from 0 to 0.20 mg.); from two to four hours, 0.01 mg. (from 0 to 0.10 mg.); from four to eight hours, 0.005 mg. (from 0 to 0.08 mg.); from eight to sixteen hours, 0.005 mg. (from 0 to 0.06 mg.); from sixteen to twenty-four hours, 0.005 mg. (from 0 to 0.15 mg.).

*Fecal Excretion of Mercury.*—The data on the fecal excretion of mercury are meager. In the case of C. F. the fecal mercury varied from 0.01 to 0.39 mg. There was no marked excretion on the day of the injection, but on the eleventh and twelfth days after the treatment was discontinued the excretion reached a level of 0.38 mg. In the case of N. N., the excretion of mercury varied from 0.01 to 0.90 mg. The figures for the excretion on the days of the injection are missing, but it is again noticeable that some time after the treatment was stopped there was still a marked excretion in the feces: 0.62 mg. three days after the cessation of treatment, 0.78 mg. eight days after and 0.90 mg. eleven days after.

*Cumulative Excretion and Retention of Mercury.*—A type patient, N. N., received four injections of 170 mg. each, totaling 680 mg. of mercury during the twenty-eight day course of treatment. The total amount of mercury excreted at the end of this period was 27.38 mg.: 15.1 mg. in the urine and 12.2 mg. in the feces, or about 4 per cent of the amount injected. In sixteen weeks the total amount excreted was about 38 mg., or about 6 per cent of the total amount injected. This indicates that a large amount of the mercury is retained in the body. Just where it is retained and whether or not it is retained in a fixed form are questionable. The fact of the increased hourly rate after several injections indicates that it might be dangerous to keep up the therapy for a sufficient length of time.

### COLLOIDAL MERCURIC SULPHIDE (MERSULFOL) BY INTRAMUSCULAR INJECTIONS

The clinical dose for the intramuscular injection of mercuric sulphide is stated as 3 cc. of the 2 per cent aqueous solution (1 cc. = 17 mg. of mercury) three times a week during the first week and twice a week thereafter. Ten cubic centimeters of the 2 per cent solution (the intravenous dose) was administered intramuscularly for five injections to the first patient in this series (fig. 8). It caused salivation during the third week. The second patient was given injections of three doses of 10 cc. each during the first week, and then the dose was decreased to 3 cc. twice a week. The other three patients were given the recommended intramuscular dose, 3 cc. (51 mg. of mercury) two or three times a week during the course of treatment.

It may be observed from the three patients who received the clinical intramuscular dose that the dose of 51 mg. is not very effective. Only in one patient, V. G. R., when the administration was continued over a period of six weeks, did the excretion reach the level of 1 mg. of mercury per day—the therapeutic effective level. In W. D. Y., who first received the larger dose and then a dose of 3 cc., it reached this level in about three weeks. In M. C. K., who received a dose of 10 cc., salivation occurred on the twentieth day. There was no case of salivation among the patients who received a dose of 51 mg.

*Daily Urinary Excretion of Mercury.*—The urinary excretion of mercury was as follows: up to twenty-four hours, 0.15 mg. (from 0 to 0.73 mg.); from twenty-four to forty-two hours, 0.11 mg. (from 0 to 0.63 mg.); three days after the injection, 0.26 mg. (from 0.07 to 0.97 mg.). In some cases there appeared to be a tendency for the excretion to increase gradually for several days after each injection.

*Hourly Urinary Excretion of Mercury.*—This was too low to reproduce, but it appeared that the excretion was highest during the first two hours. The medians for the patients who had received injections of 51 mg. of mercury were as follows: up to one hour, 0.01 mg. (from 0 to 0.03 mg.); from one to two hours, 0.01 mg. (from 0.01 to 0.06 mg.); from two to four hours, 0.005 mg. (from 0.005 to 0.02 mg.); from four to eight hours, 0.005 mg. (from 0.002 to 0.02 mg); from eight to sixteen hours, 0.005 mg. (from 0.004 to 0.01 mg.); from sixteen to twenty-four hours, 0.005 mg. (from 0.001 to 0.01 mg.); from twenty-four to forty-two hours, 0.001 mg. (from 0.001 to 0.01 mg.).

*Fecal Excretion of Mercury.*—This was generally found to be low, but on some days it was higher than the urinary excretion. In the cases of I. H. D. and J. M. O., the weekly specimens were combined for analysis, and the maximum average obtained in either case was 0.15 mg. of mercury per day; V. G. R. showed a maximum of 0.40 mg. of mercury. Even with the larger doses, the fecal excretion did not exceed 1 mg. of mercury. The highest was in the case of M. C. K., who excreted 0.92 mg. of mercury.

*Cumulative Mercury Excretion and Retention.*—A type patient, I. H. D., received eight injections of 51 mg. of mercury each, totaling 408 mg. of mercury during the twenty-eight day course of treatment. The cumulative excretion of mercury at the end of this period was 8.65 mg.: 4.42 mg. in the urine and 4.23 in the feces. This is about 2 per cent of the amount injected. In sixteen weeks the cumulative excretion was about 14 mg. of mercury, or about 3.5 per cent of the total amount injected. As in the case of intravenous injections, a large amount of mercury is retained in the body and may be a source of danger.

SYNOPSIS OF DATA

As the multiplicity of data may be confusing, it appears desirable to examine their significance from various points of view.

1. *Fecal Excretion.*—This may be dismissed with a few words. With all the compounds injected, except flumerin, it was quantitatively of subordinate importance. It did not contribute anything significant to the picture of excretion of mercury, since the biliary and intestinal excretion are less directly related to the mercurial blood concentration than the urinary excretion. With flumerin, the fecal excretion was over three times higher than the urinary excretion; being a derivative of eosin, flumerin is doubtless excreted largely by the bile.

2. *Urinary Excretion as an Index to the Blood Concentration.*—The urinary excretion must depend rather directly on the concentration of the mercury dissolved in the blood plasma, so that it must reflect the direction and, at least roughly, the degree of change in this concentration. Since the therapeutic action declines promptly when soluble mercury ceases to circulate in the blood, the urinary excretion of mercury may also be considered an index of the therapeutic potency, provided the mercury is present as an active compound.

3. *Form of the Curve for Excretion.*—Differences in the rapidity with which the urinary excretion of mercuric compounds sets in, rises and declines lead to periodicity or continuity in the curves for excretion in the various treatments. These may be arranged in four successive groups as follows:

Group A. Periodic, Rapidly and Completely Remittent: The urinary excretion declines acutely, reaching its peak in one or two hours and returning promptly to zero in from eight to twenty-four hours. This group comprises the intravenous and intramuscular injections of the more rapidly excreted organic mercuric compounds, namely (in the order of decreasing height of the peak):

Salyrgan, intravenously (fig. 5)
Novasurol, intravenously (fig. 4)
Novasurol, intramuscularly (fig. 4)
Mercuric oxycyanide, intravenously (fig. 2)

Group B. Periodic, Completely but More Slowly Remittent and Noncumulative: The urinary excretion rises rapidly to a peak but descends more slowly to near zero. This comprises injections of the following preparations in the order of decreasing completeness of remission:

Salyrgan, intramuscularly (fig. 5)
Mercurosal, intravenously (fig. 6)
Mercurosal, intramuscularly (fig. 6)
Flumerin, intravenously (fig. 7)
Colloidal metallic mercury, intravenously (fig. 7)

Group C. Periodic, Incompletely Remittent and Cumulative: The excretion also rises promptly but declines somewhat more slowly and quite incompletely, so that the excretions of the successive injections become superimposed. This comprises the intravenous and intramuscular injections of compounds which are not smoothly soluble as such, but which undergo chemical solution in the tissue, namely:

Mercuric salicylate, intramuscularly (fig. 3)
Mersulfol, intravenously (fig. 8)
Mersulfol, intramuscularly (fig. 8)
Mercuric benzoate, intramuscularly (fig. 2)
Mercuric sodium bromide, intramuscularly (fig. 2)

Group D. Continuous and Highly Cumulative: This group comprises the intramuscular injections of the difficultly soluble preparations, such as the oily suspensions of metallic mercury and mild mercurous chloride, the oral methods and the inunctions:

Mercuric oil, intramuscularly (fig. 3)
Mild mercurous chloride, intramuscularly (fig. 3)
Oral administration (fig. 1)
Inunctions (fig. 1)

4. *Level for Excretion of Mercury.*—The therapeutic and toxic effects of mercury could conceivably be influenced by three factors: the concentration attained in the blood, the time during which the concentration is maintained and the quantity which is stored in the tissues. The maximal concentration attained at any moment would be of major therapeutic importance if the action were directly parasitic, but the drug must needs be in active form, capable of liberating mercury ions. If the therapeutic action is indirect, the maintained concentration would probably be more important. Mercury stored in the tissues may or may not be important, according to whether it is stored as active soluble or as inactive insoluble compounds. Comparison of the clinical efficiency with these three factors as reflected in the excretion should therefore indicate which is chiefly concerned in the actions, and thus perhaps also give some hint of the mechanism of the therapeutic effects. Accurate quantitative methods of therapeutic evaluation are not available, but the limited knowledge that is available will be seen to give at least tentative answers.

5. *Level for Maximal Excretion.*—The factor of intensity apart from duration is represented by the maximal height of urinary excretion. This was obtained by taking the median of the three highest daily urinary excretions of mercury in each series. It is shown in column 3 of the table. The compounds fall into three groups:

(*a*) The highest group, which produces an excretion of more than 10 mg. of mercury per day, includes only the easily soluble organic

mercuric compounds, novasurol, salyrgan and mercurosal by intravenous or intramuscular injections. These are known to possess little, if any, antisyphilitic efficiency; therefore, either the effect does not depend on high concentration per se, or organically bound mercury is not efficient even in high concentration.

*Median Total Excretion and Retention of Mercury*

| Medication* | Total Amount Administered in 28 Days, Mg. of Mercury | Median Level of Daily Urinary Mercury | | | Total Mercury Excreted by the Urine in 28 Days, Mg. of Mercury | Total Mercury Retained in 28 Days, Mg. of Mercury | Percentage of Mercury Retained in 28 Days |
|---|---|---|---|---|---|---|---|
| | | During Maximal Period, Mg. of Mercury | At End of First Week, Mg. of Mercury | At the End of 28 Days, Mg. of Mercury | | | |
| **Inunctions** | | | | | | | |
| Mild mercurous chloride, 50% (43% of mercury) | 48,160 | 0.1 | 0.04 | 0.10 | 1.30 | ..... | .... |
| Oleate, 20% (4.8% of mercury) | 5,376 | 0.2 | 0.10 | 0.20 | 3.80 | ..... | .... |
| Simple, 4.6% of mercury | 5,152 | 0.2 | 0.05 | 0.20 | 2.10 | ..... | .... |
| Simple, 50% of mercury | 56,000 | 0.8 | 0.12 | 0.80 | 10.70 | ..... | .... |
| Massive, 30% of mercury | 36,000 | 0.9 | 0.27 | 0.90 | 16.10 | ..... | .... |
| **Oral administration** | | | | | | | |
| Mercuric chloride, 5 mg. × 3 | 420.0 | 0.3 | 0.07 | 0.33 | 4.57 | ..... | .... |
| Mercurous iodide 0.016 Gm. × 4 | 548.8† | 1.1 | 0.15 | 0.51† | 2.23† | ..... | .... |
| Mercury with chalk, 0.2 Gm. | 2,156.0 | 1.2 | 0.14 | 0.94 | 12.90 | ..... | .... |
| Mercury with chalk, 0.5 Gm. | 5,390.0 | 2.4 | 0.37 | 2.21 | 25.60 | ..... | .... |
| Mild mercurous chloride (Buergi) | 1,106.0 | 4.2 | 2.20 | 3.50 | 67.40 | ..... | .... |
| Mercurous iodide (Buergi) | 1,113.8 | 4.5 | 3.40 | 4.50 | 81.70 | ..... | .... |
| **Injections** | | | | | | | |
| In oil | | | | | | | |
| Mercuric oil (M) (Lomholt) | 300 | 4.4 | 0.40 | 0.9 | 41.90 | 548.2 | 91.4 |
| Mild mercurous chloride (M) (Lomholt) | 255 | 3.0 | 0.24 | 2.0 | 31.50 | 205.8 | 80.7 |
| Mercuric salicylate (M) | 240 | 5.1 | 0.34 | 2.3 | 68.50 | 165.5 | 69.0 |
| **Watery, ionizable preparation** | | | | | | | |
| Mercuric oxycyanide (V) | 59.85 | 0.7 | 0.02 | 0.1 | 3.10 | 55.8 | 93.2 |
| Mercuric benzoate (M) | 113.10 | 0.8 | 0.04 | 0.1 | 3.90 | 103.5 | 91.5 |
| Sodium mercuric bromide (M) intermittently | 49.50 | 0.5 | 0.03 | 0.4 | 2.10 | 45.7 | 92.3 |
| Sodium mercuric bromide (M) daily | 154.00 | 1.0 | 0.38 | 1.0 | 14.40 | 133.5 | 86.6 |
| **Watery, organic preparation** | | | | | | | |
| Novasurol (M) | 127.12 | 10.4 | 0.04 | 0.2 | 54.70 | 69.6 | 54.7 |
| Salyrgan (M) | 141.00 | 10.5 | 0.18 | 0.2 | 78.30 | 53.5 | 38.0 |
| Mercurosal (M) | 151.90 | 11.5 | 0.12 | 0.3 | 82.00 | 64.6 | 42.5 |
| **Watery, organic preparation** | | | | | | | |
| Novasurol (V) | 127.12 | 11.9 | 0.03 | 0.1 | 54.90 | 60.1 | 47.3 |
| Salyrgan (V) | 141.00 | 27.3 | 0.04 | 0.1 | 93.90 | 43.9 | 31.1 |
| Flumerin (V) | 260.00 | 3.0 | 0.22 | 0.3 | 15.60 | 200.5 | 77.1 |
| Mercurosal (V) | 347.20 | 23.6 | 0.30 | 0.3 | 142.40 | 201.4 | 58.0 |
| **Watery, colloidal preparation** | | | | | | | |
| Metallic mercury (V) | 450 | 0.4 | 0.02 | 0.1 | 2.70 | 443.7 | 98.6 |
| Mercuric sulphide (M) | 408 | 0.4 | 0.08 | 0.3 | 4.42 | 399.3 | 97.9 |
| Mercuric sulphide (V) | 680 | 3.0 | 0.05 | 2.3 | 15.10 | 652.6 | 96.0 |

* (M) denotes intramuscularly; (V), intravenously.
† 14 days.

(*b*) The group of lowest maximal concentration, up to 0.5 mg. of mercury per day, comprising: inunction with diluted ointments of mercury (4.6 per cent of mercury) and of the oleate (4.8 per cent of mercury) and with strong ointment (50 per cent) of mild mercurous chloride; intravenous injections of metallic mercuric suspensions; intramuscular injections of colloidal mercuric sulphide, and the oral administration of mercuric chloride—all these in the stated dosage. These doses are also ineffective against syphilis and do not produce salivation, while larger doses of the same preparations (except inunctions with mild mercurous chloride) are effective and toxic. It appears, therefore, that the maximal daily excretion must surpass a certain level—about 0.5 mg. of mercury—if effects are to be produced.

(*c*) All the effective preparations and doses belong to the intermediate group, with maximal daily urinary excretion of from 0.5 to 5 mg. of mercury. Arranged in descending order of excretion, these are:

Mercuric salicylate, intramuscularly
Mercuric oil, intramuscularly
Mild mercurous chloride, intramuscularly
Mersulfol, intravenously
Flumerin, intravenously
Mercury with chalk, 0.5 Gm. orally
Mercury with chalk, 0.2 Gm. orally
Protiodide, orally
Mercuric sodium bromide, intramuscularly, daily
  Massive 30 per cent inunction
  Simple 50 per cent inunction
Mercuric benzoate, intramuscularly
Mercuric oxycyanide, intravenously
Mercuric sodium bromide, intramuscularly, intermittently

This order does not appear to have a definite relation to therapeutic efficiency or to the tendency to stomatitis. It may therefore be concluded that the maximal concentration is not a decisive factor, and hence that the mercury is probably not a direct parasiticide.

6. *Urinary Excretion at the End of the Four Weeks' Course.*—This includes the factor of duration as well as intensity. The data (column 5 of the table) may again be arranged into several groups, as shown in the following lists. The comparison of the fourth week and of the maximal levels emphasizes the fundamental difference between these data.

Group A. Median Urinary Excretion at the End of the Fourth Week, Less Than 0.5 Mg. of Mercury per Day: The methods in this group are uniformly ineffective against syphilis and do not produce salivation. They comprise the diluted inunctions, the inunctions with mild mercurous chloride, the intravenous and intramuscular injections of

the organic mercurials, the safe dosage of the intravenous colloidal suspensions and the oral administration of mercuric chloride, as follows:

| | End of the Fourth Week, Mg. of Mercury | Maximal Level, Mg. of Mercury |
|---|---|---|
| Weak inunctions: | | |
| 50 per cent mild mercurous chloride | 0.1 | 0.1 |
| 4.6 per cent mercury | 0.2 | 0.2 |
| 4.8 per cent mercury in oleate | 0.2 | 0.2 |
| Oral administration: | | |
| Mercuric chloride | 0.3 | 0.3 |
| Injections: | | |
| Metallic mercury (intravenously) | 0.1 | 0.4 |
| Mercuric sulphide (intramuscularly) | 0.3 | 0.4 |
| Mercuric oxycyanide (intravenously) | 0.1 | 0.7 |
| Mercuric sodium bromide, intermittent (intravenously) | 0.1 | 0.8 |
| Mercuric benzoate (intramuscularly) | 0.1 | 0.8 |
| Flumerin (intravenously) | 0.3 | 3.0 |
| Novasurol (intramuscularly) | 0.2 | 10.4 |
| Salyrgan (intravenously) | 0.2 | 10.5 |
| Mercurosal (intramuscularly) | 0.3 | 11.5 |
| Novasurol (intravenously) | 0.1 | 11.9 |
| Mercurosal (intravenously) | 0.3 | 23.6 |
| Salyrgan (intravenously) | 0.1 | 27.3 |

The list is arranged in the order of ascending maximal excretion concentrations, which range between the wide limits of 0.1 and 27.3 mg. of mercury, while the excretion for the fourth week has the narrow range of from 0.1 to 0.4 mg. of mercury. This illustrates the fact that the efficiency coordinates with the excretion for the fourth week rather than with the maximal level of excretion.

Group B. Median Urinary Excretion at the End of the Fourth Week, Between 0.8 and 1 Mg. of Mercury per Day: This group comprises the active inunctions, the oral administration of mercury with chalk in doses of 0.2 Gm., the daily intramuscular injections of sodium mercuric bromide and the weekly injections of mercuric oil as follows:

| | End of the Fourth Week, Mg. of Mercury | Maximal Level, Mg. of Mercury |
|---|---|---|
| Inunctions: | | |
| 50 per cent mercury, simple | 0.8 | 0.8 |
| 30 per cent mercury, massive | 0.9 | 0.9 |
| Injections: | | |
| Mercuric sodium bromide, intramuscularly daily | 1.0 | 1.0 |
| Mercuric oil, intramuscularly | 0.9 | 4.4 |
| Oral administration: | | |
| Mercury with chalk, 0.2 Gm. | 0.9 | 1.2 |

All these methods are actively antisyphilitic, and tend to produce salivation. It appears, therefore, that this relatively low excretion is effective if it is attained by cumulation over four weeks.

Group C. Median Urinary Excretion at the End of the Fourth Week, Between 2 and 4.5 Mg. of Mercury per Day: This group comprises the oral administration of mercury with chalk in doses of 0.5 Gm., of mercurous iodide, and of mild mercurous chloride; also the intravenous injection of colloidal mercuric sulphide and the intramuscular injections of mercuric salicylate and of mild mercurous chloride as follows:

| | End of the Fourth Week, Mg. of Mercury | Maximal Level, Mg. of Mercury |
|---|---|---|
| Injections: | | |
| Mild mercurous chloride, intramuscularly | 2.0 | 3.0 |
| Mercuric sulphide, intravenously | 2.3 | 3.0 |
| Mercuric salicylate, intramuscularly | 2.3 | 5.1 |
| Oral administration: | | |
| Mercury with chalk, 0.5 Gm. | 2.0 | 2.4 |
| Mild mercurous chloride (Buergi) | 3.5 | 4.2 |
| Protiodide (Buergi) | 4.5 | 4.5 |

All these methods are clinically effective and tend to produce salivation; the tendency to salivation appears greater than that noted for the preparations in group B. It may also be presumed that the therapeutic effects occur somewhat more promptly, since an effective level is attained more rapidly, as illustrated by the excretion at the end of the first week (column 4 of the table).

*7. Cumulative Urinary Excretion of Mercury.*—The total quantity of mercury excreted in the urine by the end of the fourth week is shown in column 6 of the table. It is not as useful a criterion as the level of excretion at the end of the fourth week, which has just been discussed, since it does not distinguish between maintained and periodic excretion. It is especially valuable for comparing effective doses of the same preparations. The compounds may be grouped as follows:

Group A. Four Week Cumulative Urinary Mercury, Less Than 5 Mg.: This comprises: the weak inunctions (simple 4.6 per cent, 4.8 per cent in oleate and mild mercurous chloride, 50 per cent); the intramuscular injections of mercuric sodium bromide (intermittently), mercuric benzoate and colloidal mercuric sulphide; the intravenous injections of metallic mercury, and mercuric oxycyanide, and the oral administration of mercuric chloride. All these preparations do not produce salivation and are therapeutically ineffective in these doses, so that efficiency requires a four week cumulative excretion of more than 5 mg. of mercury.

Group B. Four Week Cumulative Urinary Mercury, from 10 to 20 Mg.: This comprises: massive 30 per cent inunctions and simple 50 per cent inunctions; the intramuscular injections of mercuric sodium bromide (daily) and mercuric sulphide; the intravenous injections of flumerin and mercuric sulphide, and the oral administration of mercury with chalk, 0.5 Gm. and 0.2 Gm.

These methods are effective against syphilis and produce salivation, so that this range of cumulative excretion suffices, if the compound contains active mercury.

Group C. Four Week Cumulative Urinary Mercury Exceeding 20 Mg.: This range includes two subgroups. (*a*) The methods employing compounds with inorganic mercury, which are highly effective therapeutically and for the production of salivation: the oral administration of mercuric iodide and mild mercurous chloride, and the insoluble injections of mercuric oil, mild mercurous chloride and mercuric salicylate. The suspensions of mercuric salicylate make a transition to the second subgroup. (*b*) The methods employing compounds with organically bound mercury, which are all at least relatively ineffective: the intravenous and intramuscular injections of salyrgan, novasurol and mercurosal. The low degree of efficiency could again be due either to the form in which the mercury is bound or to the failure to maintain adequate concentration between injections.

Aside from these organic compounds satisfactory correlation is seen to exist between efficiency—both antisyphilitic and toxic (liability to stomatitis)—and the four week level of urinary and cumulative excretion. Since both effects also increase with the duration of the course, it is improbable that the antisyphilitic action is produced by direct toxicity of the spirochete.

8. *Quantity of Mercury Retained at the End of the Treatment.*—When the administration of mercury is stopped during active syphilis, the symptoms return so promptly that the effect of the metal may be considered as practically conterminous with its administration, or rather with its absorption, which in turn coincides with the curve for excretion. It is important to inquire whether significant quantities of mercury remain in the body when the administration is discontinued and the active excretion and antisyphilitic efficiency cease, for this would show that the mercury that is retained in the tissues is therapeutically inactive, and therefore, that the therapeutic action is confined to the actively circulating diffusible mercury. The retention is, of course, measured by the difference between the amount of mercury administered and that excreted in the urine and feces. With oral administration and with inunctions the actual quantity of mercury absorbed is not known, so that these methods are excluded from consideration. This applies also to the intramuscular injections of difficultly soluble compounds; but it

may be assumed that the easily soluble compounds are practically completely absorbed, and with the intravenous injections absorption need not be considered. It is needless, and indeed theoretically misleading in this problem, to determine the excretion after the therapeutic action has ceased; practically it would not make much difference since the rate of excretion rapidly falls to very low levels. This occurs certainly within a week after the final injection of the soluble compound, so that this time has been included. It is shown in column 7 of the table. It is seen that the amount of mercury retained in the four week course varies widely for the different compounds—between 43.9 and 652.6 mg. of mercury—the largest retention occurring with the intravenous colloidal preparations. In any case, however, it represents a considerable percentage of the total mercury administered (column 8 of the table): for organic, readily excretable preparations given intravenously or intramuscularly, from 31 to 77 per cent; for inorganic soluble preparations administered intravenously or intramuscularly, from 81 to 93 per cent; for colloidal preparations given intravenously, from 96 to 99 per cent.

These quantities of mercury retained in the tissues are of course larger than the total mercury in active circulation, so that it appears that the stored "cellular" mercury is therapeutically ineffective; it is probably undesirable, since it is not possible to say whether it is always entirely harmless.

9. *Clinical Correlations.*—The far-reaching concordance of the data for excretion with the clinical effects justifies the concurrent use of both to supplement each other. The study of excretion supplies a quantitative basis for the rather qualitative clinical picture and justifies the presumptive ranking of treatments that have not been adequately studied in the clinic. It should be useful by concentrating the clinical study on more promising compounds. It is therefore helpful to recapitulate the studies on excretion from the clinical standpoint.

The studies on excretion show that the antisyphilitic effects demand a maintained circulation of dissociable and diffusible mercury at adequate concentrations, which may be defined as reflected in a level for urinary excretion of from 0.8 to 1 mg. of mercury per day at the end of the four week course. Conversely, the immobilized mercury that is stored in the tissues, nondissociable organic combinations of mercury and the very brief concentrations that are attained by intravenous injection appear useless against syphilis. Furthermore, all the clinical treatments that have proved practically useful reach the effective concentration by a gradual, cumulative rise, presumably because this is the safest device for securing an adequate maintenance. The progressive cumulation justifies the intermission in mercurial treatment, which has been the usual clinical rule; this prevents an excessive rise of the level for mer-

cury and also gives an opportunity for the tissues to recover from any damage that the mercurial irritation may have inflicted on them. However, this period of intermission should probably be occupied with arsenical therapy—certainly in all acute syphilis—to prevent a recrudescence of the spirochetal infection and a subsequent relapse.

The fact that the concentration of mercury is attained gradually and that it may be maintained for some time after the full therapeutic effect is reached militates against the use of mercury as a "drug of attack" in the acute stage of syphilis, i. e., in the seronegative primary stage. This stage calls for the arsphenamines, or, if these are not tolerated, for bismuth compounds, which act more promptly. If mercury is used in this stage, however, it should be given by daily injections of dissociable solutions—corrosive mercuric chloride, biniodide or succinimide—or perhaps by the biweekly administration of mercuric salicylate.

The usefulness of mercury is chiefly as a "drug of consolidation" i. e., for holding the ground between the arsenical treatments, and in this its maintained concentration is the decisive factor. This is reflected in the level of urinary excretion at the end of the mercurial course, and the level at the end of the fourth week has been taken for comparison. From our data it appears that less than 0.5 mg. of mercury per day is inadequate. This should exclude inunctions with ointments of mild mercurious chloride and of 5 per cent mercury or oleate, the biweekly injections of mercuric oxycyanide, mercuric benzoate, flumerin and colloidal mercury, both intramuscularly and intravenously, and also the oral administration of mercuric chloride in the ordinary dosage. It also excludes the organic mercuric compounds, salyrgan, novasurol and mercurosal; these give a very high urinary excretion for one hour after the injections, but the level for excretion drops almost to zero within a few hours. For instance, the median hourly urinary excretion of mercury after the intravenous administration of salyrgan is 27.3 mg. of mercury in the first hour, and for mercurosal, 23.6 mg. of mercury, but by the end of the week it has fallen to 0.04 mg. and 0.3 mg. of mercury respectively. The early excretion produces the prompt diuretic action which is utilized in edema, but the antisyphilitic action is probably low, because the concentration is not maintained.

Definite antisyphilitic efficiency is seen in the level for the fourth week of from 0.8 to 1 mg. of mercury per day, and this excretion appears sufficient. Methods which lead to higher levels for four week periods; from 2 to 4.5 mg. of mercury may be more promptly effective, but their ultimate efficiency is probably no greater, since usually these higher levels cannot be maintained as long because of the onset of stomatitis. The level from 0.8 to 1 mg. comprises most of the currently popular methods: the classic daily rotation inunction with strong mercurial ointment, the weekly massive inunctions with 30 per cent oint-

ment, the oral administration of mercury with chalk, 0.2 Gm. per day, the intramuscular injections of the soluble dissociable compounds, the biniodide, bichloride and succinimide, and mercuric benzoate and perhaps the intravenous injection of flumerin. It includes also the injections of mercuric oil. However, the absorption of the last-mentioned preparation is subject to sudden exacerbations which in our experience have resulted in several fatalities, so that we have abandoned its use.

The level of from 2 to 4.5 mg. of mercury includes certain injections and oral administration. The injections are those of mild mercurous chloride, of colloidal metallic mercury and mercuric sulphide intravenously and of mercuric salicylate. The relatively high level for the last-mentioned preparation is due to the fact that the major part is excreted promptly as organic mercury, but a sufficient amount is broken down to be effectively antisyphilitic. The injections of mild mercurous chloride are highly effective but painful. The intravenous injections of colloidal metal are excreted unevenly, since they must be converted into dissociable compounds after being in large part caught and deposited in the reticular system. Such uncontrollable variations are undesirable and perhaps dangerous, and the lasting deposition of such large amounts of mercury in the tissues may not be indifferent. The intramuscular injections of colloidal suspensions largely obviate the latter objection, but they also produce a variable excretion and seem rather undesirable.

Oral administration of mercury with chalk, mercurous iodide, mercuric chloride and mild mercurous chloride were advocated by the famous syphilographers of the last century; the "gray powder," by Jonathan Hutchison, and the protiodide, by Fournier. They went out of vogue when the injections became popular; perhaps chiefly because the administration is done by the patient and is therefore difficult to control. There is also a tendency to local intestinal symptoms, especially with mild mercurous chloride, and clinical evidence of greater liability to severe stomatitis, disproportionate to the therapeutic effect. Clinicians who formerly used the protiodide extensively generally recall profusely salivated patients, with a mouthful of mucous patches. The persistence of these lesions may have been due to a less effective use of arsphenamine at that time, and possibly to a rapid development of stomatitis before the therapeutic effect was attained, for with oral administration it is possible to reach an excessive level of excretion rather rapidly. If these explanations are correct, the objectionable features should be avoidable and the oral method could be made quite useful. It is certainly capable of smoothly securing an effective level of excretion, often with little trouble to the patient. The significance of salivation in general deserves further consideration. In general, it appears that salivation may occur either quite early, or after two or three weeks. The early stomatitis has little relation to the dosage or concen-

tration of the mercury, and may be attributed either to "mercurial susceptibility" or to the virulence of the invading organism which may take advantage of even a slight mercurial injury. The latter appears to be a correct explanation, since the stomatitis generally affects practically all the mercury-treated patients in the ward at the time. It has therefore little relation to the concentration of the mercury. The stomatitis which develops after two or three weeks has a more definite relation to the concentration of mercury.

The fecal excretion of the mercury has not been found of any clinical significance, except possibly with flumerin, which is largely excreted by the feces, presumably through the bile, since it is a derivative of eosin. This suggests the possibility that it might be especially useful in hepatic syphilis. However, it may not be affirmed *a priori* that the excretion of a drug by the liver adds to its antisyphilitic action in this situation, for this is probably of no importance if the antisyphilitic action of mercury is other than directly antiseptic.

10. *Further Developments in Mercury Therapy.*—The indispensable conditions of effective antisyphilitic mercurial medication resolve themselves into the continuous maintenance of an adequate concentration of dissociable and diffusible mercury. Since diffusible mercury is rapidly excreted, the maintenance of a continuous level requires continued absorption. This can be secured by frequent administration or, more conveniently, by the establishment of depots from which absorption takes place between administrations. It is secured quite effectively by the current clinical methods, and further improvements are likely to be confined to details of convenience, mitigation of local irritation and, if possible, greater uniformity of absorption, permitting more accurate dosage. Analytic methods by which the concentration of the mercury in the urine and preferably in small amounts of blood could be checked clinically more promptly and conveniently than is now the case would be a significant improvement.

It is at least equally important to realize the directions which would *not* lead to improvements:

It appears unpromising to raise the concentration of dissociable mercury in the blood above the present limits, either temporarily or continuously, for this increases the injurious effects of mercury out of proportion to the therapeutic effects.

It appears useless to make further trials with compounds which hold their mercury in firm organic combination.

It appears useless to attempt to keep the mercury "perfectly" under control, for the depots which are necessary for maintaining a continuous absorption necessarily imply some sacrifice of control.

It appears useless to emphasize the rapid elimination from the blood stream, for this occurs with all compounds.

It appears useless to attempt to "saturate" the tissues with mercury, for while the tissues retain surprisingly large quantities of mercury in all methods of administration, this mercury retained in the tissues is therapeutically inactive until it is remobilized, and this occurs too slowly to attain effective levels. On the other hand, the mercury may not be harmless to the tissues.

It appears unpromising to establish deposits in organs by the injection of colloidal mercurial solutions. This may be done, but the conversion is variable and beyond control.

## CONCLUSIONS

A study of the excretion of mercury after the injection of a variety of mercuric compounds and a comparison of injection with the oral and inunction methods lead to the following conclusions:

1. The antisyphilitic efficiency of mercurial treatment appears to be conditioned on the continued maintenance of an adequate concentration of diffusible, dissociable mercury. The mercury that is fixed and stored in the tissues appears to play no therapeutic rôle.

2. The urinary excretion of mercury serves as an indicator of the diffusible mercury. The fecal excretion is unimportant, qualitatively and quantitatively, except for injections of flumerin.

3. The urinary curve for excretion ranges from periodic, with the injection of the diffusible organic compounds, to continuously cumulative, with methods employing the less soluble compounds which form absorption depots, including inunctions, oral administration and intramuscular injections of slowly soluble or precipitant compounds.

4. All the effective antisyphilitic methods show the continuously cumulative type of excretion.

5. In accordance with this the closest correlation exists between the antisyphilitic efficiency and the level for daily urinary excretion toward the end of the treatment (in this series, the end of the fourth week).

6. All forms of treatment yielding levels below 0.5 mg. of mercury per day at the end of the fourth week are clinically ineffective. These include: the inunctions with ointments of mild mercurous chloride and with weak (5 per cent) ointments of metallic mercury and mercury oleate; the oral administration of mercuric chloride in doses of 15 mg. per day; the intravenous injections of oxycyanide, and the intramuscular injections of the benzoate in the usual dosage; intermittent intramuscular injections of biniodide, and intravenous injections of compounds with their mercury in firm organic combination—salyrgan, novasurol and mercurosal. These give very high temporary levels for excretion of mercury, but they sink to insignificant ones within a few hours.

7. All methods of treatment which secure a daily urinary excretion of from 0.8 to 1 mg. of mercury at the end of the fourth week are effectively antisyphilitic and may cause stomatitis. The ordinary and the massive inunctions, the oral administration of 0.2 Gm. of mercury with chalk, daily, the daily intramuscular injection of mercuric sodium bromide and the weekly intramuscular injection of mercuric oil come within this group. With the last preparation there is the constant danger of cumulative intermittent absorption and intoxication.

8. The oral administration of protiodide and mercuric sodium bromide, 0.5 Gm. per day, and some of the methods of injection raise the level for the fourth week to 2 or 4.5 mg. of mercury per day. These higher levels probably act more rapidly against syphilis, but they are also more likely to produce severe stomatitis, which limits their continuance and reduces their efficiency.

9. Considerable quantities of mercury are retained in the tissues indefinitely, even with the intravenous injections of diffusible organic compounds (from 31 to 77 per cent); these retentions are especially high with the colloidal solutions (from 96 to 99 per cent).

10. Since the antisyphilitic action ceases promptly with the excretion, this retained mercury is therapeutically useless. It is undesirable, since it may not be harmless to the tissues.

# MYCOSTATIC STUDIES ON CERTAIN MONILIAE AND RELATED FUNGI

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The purpose of this experiment was to study the mycostatic action in vitro of certain dyes, especially crystal violet and its compounds gentian and methyl violet, and of some other chemical substances more or less representative of the ones used in the treatment of dermatomycosis. The list is by no means complete.

The work was planned in three parts: classification of the organisms used in the experiment, action of dyes and chemicals and effect of irradiation and of irradiation plus sensitization on yeastlike fungi and related organisms. The results of the first and last parts of the work are reported in another paper.

## CLASSIFICATION

A careful study and classification of the organisms used in any test are absolutely necessary whenever comparisons are to be made and reliable results are desired. My co-workers and I followed the classifications of Sabouraud, Guillermond, Vuilemin, Castellani, Henrici and other authors. Forty-one organisms were collected from various sources and were classified according to their morphology and cultural characteristics as follows: ten strains of Monilia, four of Torula, eight of Saccharomyces, four of Trichophyton, eleven of Epidermophyton, three of Zygosaccharomyces and a doubtful one of Endomyces.

## ACTION OF DYES AND CHEMICALS

The bacteriostatic and bactericidal action of the dyes and chemicals in vitro has been reported on several times, but these reports indicate that different methods have been employed. A uniform technic should be used in order to facilitate the comparison of results.

In our tests twenty-four hour culture was always used. In this period of time no one of the spore-forming fungi produced endospores. A uniform suspension of vegetative budding cells equally exposed to the action of the chemical was obtained in all the strains of organisms used in the test, although they represented different genera and species which in their later stages of growth differ widely in morphology.

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The work was made possible through the American Association of University Women, which granted me the Latin-American Fellowship for 1933 and 1934. It was done under the supervision and with the help of Dr. Calista Eliot and Dr. B. Hampil of the Department of Bacteriology of the Johns Hopkins School of Hygiene.

*Mediums.*—After careful work with several mediums we found that all the fungi used in the experiment gave an abundant and uniform growth in dextrose broth (plain or extract broth plus 1 per cent dextrose at a $p_H$ of 7 or 7.2) at a temperature of 34 C. in a period of time shorter than that required for good growth in Sabouraud's or any other medium. Epidermophyton and Trichophyton produced perfectly separated colonies that were easily transferred. The same broth was used in the preparation of the cultures for the test, for the dilutions of the dye (except the stock solution), for the controls and for subcultures. Most of the fungi fermented dextrose with the production of acid, reducing the broth from $p_H$ 7.2 to about $p_H$ 6.6. This fact was taken into consideration in some of the tests, but since it was true for all tests and controls the error introduced was fairly uniform. Lactose broth with a $p_H$ of from 7.4 to 7.6 was used in an attempt to study the influence of alkalinitity, because no one of the fungi used produced acid when this sugar was added to the plain broth. The growth obtained in lactose broth, however, was not as abundant and uniform as that obtained in dextrose broth; the results were inconclusive.

*Number of Cells.*—The number of cells in the unit volume of 0.1 cc. of a twenty-four hour culture was obtained by a direct counting in a red blood cell counting chamber. Other methods advised did not give as uniform results. The cell counts for the strains of Torula varied rather widely. A low count was 18,160,000 cells per cubic millimeter, and a high count, 63,600,000; the average count for all strains of Torula was about 40,880,000. The cell counts for each strain of Saccharomyces, on the other hand, were very uniform and even the cell counts for different species varied little. Counts of 3,848,000, 3,852,000 and 3,244,000 were representative, with an average of 3,414,000. The strains of Monilia showed lower counts with more variations, such as 1,768,000, 1,956,000 and 4,616,000, with an average of 2,843,000.

*Tests.*—Germicidal Test: The germicidal test with crystal violet was made according to the standard methods of testing disinfectants. For each culture a set of tubes was prepared with crystal violet in dilutions of 1: 10,000, 1: 15,000 and 1: 20,000 in dextrose broth. One-tenth cubic centimeter of a twenty-four hour culture was added to each tube; the contents were shaken and kept at the optimum temperature of 34 C. in a water bath. In order to know whether an amount of dye sufficient to kill the organism was transferred in the subcultures a control tube was prepared. Subcultures were made after the organisms were exposed for thirty and sixty minutes to the dilutions of the dye which had been previously kept in the water bath at 34 C. These subcultures in dextrose broth were incubated at the optimum temperature and kept under the best conditions for growth for several days. Not all of the cultures were tested, but the repeated results with the ones used indicate that the action of crystal violet on fungi in high dilutions is not so much germicidal as it is germistatic. Strains of Monilia and Torula were killed in thirty minutes in dilutions of 1:10,000. All the strains of Saccharomyces were killed in the same dilution in sixty minutes and most of them (five strains) in thirty minutes. All the other fungi (Epidermophyton and Trichophyton) grew in the subcultures after sixty minutes' exposure to dilutions of the dye of 1: 20,000. It is clear that no specificity was shown in the germicidal test.

Germistatic Test: This test was made for the purpose of finding the highest dilution of a dye or chemical that completely inhibits the growth of the fungi not only in twenty-four hours but for as long as seven or fifteen or more days when maintained under the most favorable conditions for their growth. A stock

dilution of the dye to be tested was made in distilled water in a sterile bottle and was kept in the icebox to avoid any evaporation. Dextrose broth was prepared in bottles in amounts of 100 cc. The dye was diluted in the bottle of broth ten times stronger than the final dilution to be tested; i. e., for a test of a 100,000 dilution, the stock dilution was diluted 1: 10,000. One cubic centimeter of this dilution was pipetted into a number of tubes equal to the number of cultures to be tested. Then 9 cc. of the dextrose broth was pipetted into each tube and mixed well with the dilution. The contents were incubated overnight to test the sterility. The next day 0.1 cc. of a twenty-four hour dextrose broth culture was added to each tube, and the contents were shaken and mixed well. After incubation for twenty-four hours at the optimum temperature of 34 C. the results were recorded, but the tubes were kept at the same temperature for at least ten days in case no growth was observed. A tube of dextrose broth plus 0.1 cc. of the culture serves as a control on the growth of the fungus and may be used as the seed culture for the following test. When owing to the intense color of the dye it was difficult to observe the growth of the organism, transfers of 1 and 0.1 cc. were made from the tube into dextrose broth. If no growth was observed but there was sediment at the bottom of the tube a drop of the sediment was spread on a plate of Sabouraud's medium. These subcultures really serve as germicidal tests in such cases in which it is difficult to decide between growth or sediment from a heavy inoculum.

## RESULTS

Eighteen chemical compounds were used in the experiment. Ten dyes—crystal violet, gentian violet, methyl violet, acid fuchsin, brilliant green, thionine, methylthionine chloride, U. S. P. (methylene blue), acriflavine and eosin—and eight substances generally used as disinfectants—mercurochrome, corrosive mercuric chloride formaldehyde, tincture of iodine, trinitrophenol, salicylic acid, phenol and cresol—were employed.

*Triphenylmethane Dyes.*—Crystal Violet: The material used had a dye content of 85 per cent. The growth of all the strains of Monilia and Torula was completely inhibited in dilutions of 1: 1,000,000; the growth of the strains of Trichophyton and Epidermophyton was inhibited in dilutions of 1: 400,000; most of the strains of Saccharomyces grew in dilutions of 1: 400,000; all but one were inhibited in dilutions of 1: 100,000. A marked specificity or selective activity for Monilia and Torula is a clearcut result.

Gentian Violet: This dye is a poorly defined mixture of violet rosaniline. Gentian violet is a mixture of crystal and methyl violet, but one must also realize that crystal violet is a component of all the deeper shades of methyl violet. The material used for this test had a dye content of 74 per cent. The growth of all the strains of Monilia was inhibited in dilutions of 1: 1,000,000; most of the strains of Torula and all of the strains of Saccharomyces, Epidermophyton and Trichophyton grew in dilutions of 1: 400,000, but not in dilutions of 1: 100,000.

Methyl Violet: The various mixtures known as methyl violet vary from reddish to bluish according to the relative amount of the more or less completely methylated compound present in the mixture. R indicates the reddish shades and B the bluish shades. The dye content of the material used by us was not specified. This dye proved less effective than gentian violet since even the strains of Monilia grew in the dilution of 1: 1,000,000. The growth of all of the strains of Monilia was inhibited, however, by a dilution of 1: 800,000; that of the strains of Torula, Saccharomyces, Epidermophyton and Trichophyton was inhibited in dilutions of 1: 100,000, but not in dilutions of 1: 400,000.

Brilliant Green: The dye content of the material used by us was not stated. The growth of all the strains of Monilia and Torula was inhibited in dilutions of 1:200,000; the strains of Saccharomyces, Epidermophyton and Trichophyton grew well in this dilution. The growth of all the fungi tested was inhibited in dilutions of brilliant green of 1:100,000. Specificity for the strains of Monilia and Torula was observed, although the difference in dilutions was not so marked as in the crystal violet. It was noticed that this dye usually inhibited the growth of the fungi in the first three or four days of incubation but that the growth was rather good after the fifth day. For this reason the test was repeated several times, and the results were always the same as those obtained in the first test.

Acid Fuchsin: This is an acid dye which owes its acid character to the fact that it is a sulphonated derivative of basic fuchsin. This dye produced a marked stimulation of growth of all the four groups of fungi tested in a dilution as low as 1:750. When acid fuchsin was added to Sabouraud's agar in an amount enough to give a dilution of 1:2,500, a luxuriant growth of all four types of fungi was obtained both in the streaked and in the poured plates after twenty-four hours of incubation at 34 C.

*Quinone-Imide Dyes.*—Thionine: This is a very strongly basic dye because of the two amino groups. Added to the dextrose broth it produced marked stimulation of growth, even in dilutions of 1:500.

Methylthionine Chloride: This dye is a salt of tetramethyl thionine. As in the case of thionine, the dilutions of 1:500 gave a very deep color to the broth and no growth could be observed. Subcultures made after twenty-four hours and three days of incubation showed a good growth of all the organisms, indicating low mycocidal and mycostatic effect. Methylthionine chloride was used as a sensitizer in combination with irradiation, giving good results.

*Xanthine Dyes.*—Acriflavine: This is a yellow basic dye developed by Ehrlich for its therapeutic value. It is used today as a disinfectant and is well known by its powerful action on certain gram-negative organisms such as Neisseria. The material used by us was acriflavine base. We found that it inhibited the growth of Saccharomyces in dilutions of 1:10,000 and completely killed this fungus after four days in the same dilution. Subcultures did not show any growth. Strains of Epidermophyton and Trichophyton as well as Monilia grew in dilutions of 1:5,000 but not in lower dilutions. It is interesting to note that apparently acriflavine has a selective action for Saccharomyces and does not inhibit the growth of Monilia in as great dilution as does crystal violet. However, the difference in effective dilutions is not so high as in crystal violet.

Eosin: This is an acid dye, considered to be tetrabromfluorescein. In dilutions of 1:500 and 1:1,000 it apparently stimulates growth. When used as sensitizer it inhibits the growth of nonpigment-forming Trichophyton after relatively long exposures.

*Chemicals and Disinfectants.*—Mercurochrome: Knowing that mercurochrome has been used in the treatment of fungus infections, we thought that this compound might be effective in relatively high dilutions. To our surprise the organism grew luxuriantly in dilutions of 1:20,000 and 1:10,000; on making the test with lower dilutions we obtained very good growth in dilutions of 1:500 and after twenty-four hours' incubation at 34 C. It is an active sensitizer to the action of visible light, as it could be observed not only in irradiation of the organisms but in the treatment of two patients with fungus infection.

Corrosive Mercuric Chloride: The growth of all of the fungi tested with this substance was inhibited in dilutions of 1:5,000; in dilutions of 1:10,000 the same result was obtained, except with two strains in which growth was doubtful. It is well known that all organisms of this group produce acid in dextrose broth, the $p_H$ of which after twenty-four hours' incubation with the organism varies from 7.2 to 6.6, and for this reason the results obtained are uniform.

Formaldehyde: The material used was commercial formaldehyde, from 35 to 40 per cent solution (as labeled). It was considered as a 35 per cent solution in making the dilutions for the test. Apparently formaldehyde is least harmful to Monilia. In dilutions of 1:2,500 strains of this organism grew well after twenty-four hours and exhibited a luxuriant growth after four days. None of the strains of Saccharomyces grew in this dilution, the growth of all the strains being inhibited in dilutions of 1:5,000 and some even in dilutions of 1:10,000. The growth of strains of Epidermophyton and Trichophyton was inhibited in dilutions of 1:2,500, but no test was made in greater dilution to find the one at which they could grow.

Tincture of Iodine: The material used contained 83 per cent alcohol, and was made according to the formula in the "Pharmacopoeia of the United States of America." Tincture of iodine did not show any inhibitory action on the strains of Monilia, Torula, Epidermophyton and Trichophyton tested, even in dilutions of 1:100, but it inhibited the growth of the strains of Saccharomyces in the same dilution. The growth of all the fungi was inhibited in dilutions of 1:50, and the fungi grew luxuriantly in a 1:200 dilution.

Trinitrophenol: This compound was used in dilutions of 1:5,000; the effect was one of stimulation, as good growth was observed after twenty-four hours' incubation at 34 C. Trinitrophenol inhibited the growth of strains of Epidermophyton and Trichophyton in dilutions of 1:1,000, but not of the other fungi tested, thus showing a specificity similar to salicylic acid.

*Physicochemical Disinfectants.*—Salicylic Acid: This acid has been used with success in treatment in the form of an ointment containing from 5 to 15 per cent of the acid. Salicylic acid showed specificity for Epidermophyton and Trichophyton because these organisms did not grow at all in dilutions of 1:1,000, while strains of Monilia, Torula and Saccharomyces grew in dilutions of 1:750 and even in dilutions of 1:500. No lower dilutions of the acid could be tested owing to its solubility.

Phenol: This preparation in a dilution of 1:100 inhibited the growth of all the fungi tested; all grew luxuriantly in dilutions of 1:1,000.

Cresol: The test with cresol revealed fungicidal properties. A solution of 1:250 was used. One cubic centimeter of a twenty-four hour culture of the organism was mixed in Petri dishes with 20 and 10 cc. of the cresol solution. Cultures of 0.1 cc. of the mixture were made after one-half minute, one minute, etc., up to fifteen minutes. No growth was obtained in any one of the dextrose broth cultures even after ten or more days of incubation, while the controls of the cultures grew well.

## TREATMENT

In a case of monilial paronychia (1930) which had been resistant for a period of two years to more than ten different types of treatment, the standard gentian violet solution was used in the gram stain, with striking results. The five fingers affected were cured in two months and no relapse has occurred up to the time this report is written. Not

TABLE 1.—*Summary of Mycostatic Tests to Show the Selective Action of Certain Dyes and Chemicals on Several Types of Fungi*

| | Dyes | | | | | | | | | | Chemicals | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Crystal Violet | | Gentian Violet | | Methyl Violet | | Brilliant Green | | Acriflavine | | Formaldehyde | | Tincture of Iodine | | Trinitrophenol | | Salicylic Acid | |
| Monilia Strain No. | 1:400,000 | 1:1,000,000 | 1:400,000 | 1:1,000,000 | 1:400,000 | 1:1,000,000 | 1:100,000 | 1:200,000 | 1:5,000 | 1:10,000 | 1:2,500 | 1:10,000 | 1:100 | 1:200 | 1:1,000 | 1:5,000 | 1:1,000 | 1:5,000 |
| 754 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 2004 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 2117 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 349 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 360 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 350E | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 752 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 2113 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 750 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| 2112 | − | − | − | − | − | + | − | − | + | + | + | + | + | + | + | + | + | + |
| Torula | | | | | | | | | | | | | | | | | | |
| 278 | − | − | − | + | − | + | − | − | − | + | − | + | − | + | + | + | + | + |
| 354 | − | − | − | + | − | + | − | − | − | + | − | − | − | + | + | + | + | + |
| 268 | − | − | − | + | + | + | − | − | − | − | − | + | − | + | + | + | + | + |
| 277 | − | − | + | + | + | + | − | − | − | − | − | + | − | + | + | + | + | + |
| 1357 | − | − | + | + | + | + | − | + | − | − | − | − | − | + | + | + | + | + |
| Saccharomyces | | | | | | | | | | | | | | | | | | |
| 358 | − | − | + | + | + | + | − | + | − | − | − | − | − | + | + | + | + | + |
| 351 | + | + | + | + | + | + | − | + | − | + | − | + | − | + | + | + | + | + |
| 353 | + | + | + | + | + | + | − | + | − | + | − | + | − | + | + | + | + | + |
| 355 | + | + | + | + | + | + | − | + | − | − | − | − | − | + | + | + | + | + |
| 182 | + | + | + | + | + | + | − | + | − | + | − | + | − | + | + | + | + | + |
| 356 | − | + | + | + | + | + | − | + | − | − | − | − | − | + | + | + | + | + |
| 280 | + | + | + | + | + | + | − | + | − | + | − | + | − | + | + | + | + | + |
| Trichophyton | | | | | | | | | | | | | | | | | | |
| I | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| II | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 1043 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 1870 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| Epidermophyton | | | | | | | | | | | | | | | | | | |
| 3 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 4 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 5 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 7 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 8 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 9 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 11 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 12 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 1611 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 1850 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |
| 1869 | − | + | + | + | + | + | − | + | + | + | − | 0 | + | + | − | + | − | + |

− indicates no growth after seven days' incubation at 34 C.; +, growth within seven days at 34 C.; 0, not done.

all the fingers were treated at the same time. A second patient with onychia, apparently due to Trichophyton, was cured after five applications of crystal violet solution at intervals of from five days to one week, in February 1934. No relapse has been reported. Therapeutic experiments with animals (five guinea-pigs and one rabbit) have been unsuccessful because these animals are immune to the infection or are cured spontaneously. Six cases of "athlete's foot" seem to be cured following

TABLE 2.—*Summary of the Tests with Certain Dyes and Chemicals Which Show No Selective Action on Several Types of Fungi*

| | | Acid Fuchsin | Thionine | Methyl-thionine Chloride | Eosin | Mercuro-chrome | Corrosive Mercuric Chloride | | Phenol | |
|---|---|---|---|---|---|---|---|---|---|---|
| Monilia | Strain No. | 1:1,750 | 1:500 | 1:500 | 1:500 | 1:500 | 1:10,000 | 1:20,000 | 1:100 | 1:1,000 |
| | 754 | + | + | + | + | + | — | + | — | — |
| | 2004 | + | + | + | + | + | — | + | — | — |
| | 2117 | + | + | + | + | + | — | + | — | + |
| | 349 | + | + | + | + | + | — | + | — | + |
| | 360 | + | + | + | + | + | — | + | — | + |
| | 350E | + | + | + | + | + | — | + | — | + |
| | 752 | + | + | + | + | + | — | + | — | + |
| | 2113 | + | + | + | + | + | — | + | — | + |
| | 750 | + | + | + | + | + | — | + | — | + |
| | 2112 | + | + | + | + | + | — | + | — | + |
| Torula | | | | | | | | | | |
| | 278 | + | + | + | + | + | — | + | — | + |
| | 354 | + | + | + | + | + | — | — | — | + |
| | 268 | + | + | + | + | + | +* | + | — | + |
| | 277 | + | + | + | + | + | | — | — | + |
| Saccharomyces | | | | | | | | | | |
| | 357 | + | + | + | + | + | — | + | — | + |
| | 358 | + | + | + | + | + | — | + | — | + |
| | 351 | + | + | + | + | + | — | + | — | + |
| | 353 | + | + | + | + | + | — | + | — | + |
| | 355 | + | + | + | + | + | +* | + | — | + |
| | 182 | + | + | + | + | + | — | + | — | + |
| | 356 | + | + | + | + | + | — | + | — | + |
| | 280 | + | + | + | + | + | — | + | — | + |
| Trichophyton | | | | | | | | | | |
| | I | + | + | + | + | + | — | + | — | + |
| | II | + | + | + | + | + | — | + | — | + |
| | 1043 | + | + | + | + | + | — | + | — | + |
| | 1870 | + | + | + | + | + | — | + | — | + |
| Epidermophyton | | | | | | | | | | |
| | 3 | + | + | + | + | + | — | + | — | + |
| | 4 | + | + | + | + | + | — | + | — | + |
| | 5 | + | + | + | + | + | — | + | — | + |
| | 7 | + | + | + | + | + | — | + | — | + |
| | 8 | + | + | + | + | + | — | + | — | + |
| | 1611 | + | + | — | + | — | — | + | — | + |

* Doubtful; no growth in the transfers.

treatment with a crystal violet preparation, but nothing can be assured before a reasonable length of time indicates that there are no relapses.

## COMMENT

Any investigation with organisms causing mycotic infections requires the use of several types of fungi and a complete study and identification of each strain before valid comparison can be made or reliable conclusions can be drawn. The classification adopted by us is based not only

on the morphologic characteristics of the cells as seen in the lesions and in culture but on their ability to produce spores and mycelia, on their fermentation activities and on certain characteristics of the cells of each genus. Not much could be done in regard to the lesions produced by these organisms because experiments with animals gave negative results. This is one of the most valuable factors because the infection produced by any one strain may vary in its manifestations or apparently similar infections may be produced by different organism. Personal experience has shown that a strain of Epidermophyton isolated from a case of "athlete's foot" may cause infection of the hair or typical tinea.

In any germistatic or germicidal test a well planned technic is necessary to obtain uniform results, time and temperature being of great importance. The most favorable conditions for the growth of the organisms must be found in order to avoid misinterpretation of the action of the substance under experiment. The test cultures must be standardized under the conditions of the experiment. The mycostatic action of the chemicals has been studied in vitro in this series with young cultures of the fungi in order to obtain a uniform type of cells and to enable us to make valid comparisons and to draw more reliable conclusions, but this work is by no means complete. It must be repeated with old cultures to study the action of the dyes and chemicals on the more resistant cells and on spores, although it must be remembered that as a rule spores are not frequently found in the lesions (Beauverie[1]).

The most striking result we obtained was the marked specific action or selective activity of crystal violet and its compounds gentian and methyl violet for fungi of the genera Monilia and Torula, the growth of which was inhibited in dilutions of 1 : 1,000,000, as compared with the action on strains of Saccharomyces, Epidermophyton and Trichophyton, the growth of which was inhibited by dilutions of 1 : 400,000 or less. This specificity may be used as a means of differentiation of Monilia from other "yeastlike" pathogenic fungi in the preliminary test for identification. We took advantage of this specificity in the study of the cultures obtained later in the course of these experiments. Crystal violet, being a definite chemical compound, was the most readily standardized and the highest in dye content of the three violet dyes used.

The triphenylmethane dyes have long been recognized for their germicidal and germistatic activities. Our experiments with crystal violet and its compounds gentian and methyl violet and with brilliant green indicate that these dyes in high dilutions inhibit the growth of organisms such as fungi imperfecti, Monilia, Torula, Saccharomyces and Epidermophyton. Acid fuchsin seems to stimulate the growth of the same type

1. Beauverie: J. Soc. de biol. **5**:80, 1917.

of organisms even in strong concentrations, but in an experiment by Schamberg and his co-workers [2] it was found that mercuric basic fuchsin proved to be a good fungicide in some of their tests. We consider that this fungicidal activity could be due to the molecules of mercury present in the compound, although basic fuchsin alone is good.

Dyes of the quinone-imide group, such as thionine and methylthionine chloride, apparently stimulate the growth of organisms causing dermatomycosis when cultivated in dextrose broth containing one of these dyes. Methylthionine chloride has been used empirically and with good results in the treatment of thrush, a moniliasis. We did not find any record in the literature about its effects. Eosin produces similar stimulating effects. Both eosin and methythionine chloride were used as sensitizers in the experiments with light. We found the latter to be more effective, especially on nonpigment-forming strains.

Acriflavine, used for its activity on certain gram-negative organisms, showed selectivity for Saccharomyces; that is, growth was inhibited in dilutions of 1:10,000, in which Monilia and Torula grew well.

Among the chemical compounds used, mercurochrome was the most interesting. Its fungistatic action is not great, but certainly it is a powerful sensitizer to visible light. Probably the entirely different results obtained in the experiments by Schamberg and Kolmer were due to a different exposure of the cultures to light. In two of three cases exposure of the lesions to visible light for fifteen minutes after the application of mercurochrome proved effective. No record of the results was obtained in the third case.

Certain disinfectants, such as tincture of iodine, which are considered of value because of their mycocidal action in the treatment of infections did not show such activity in the in vitro tests, but the formaldehyde and tincture of iodine showed selectivity for Saccharomyces. Phenol proved to be effective only in low dilutions. Cresol was found to be a good fungicide. Salicylic acid proved to be more effective on Epidermophyton and Trichophyton than on Monilia and other fungi imperfecti.

In the treatment of dermatomycoses, such as paronychia, onychia and "athlete's foot," crystal violet proved to be effective. Owing to the impossibility of producing a well defined infection in laboratory animals, not very much can be said about the therapeutic value of crystal violet. More experimental work on infections in man must be done.

## CONCLUSIONS

1. Crystal violet and its compounds, gentian and methyl violet, showed marked specific action or selective activity in vitro on fungi of

2. Schamberg, J. F.; Brown, H., and Harkens, M. J.: The Chemotherapy of Ringworm Infection, Arch. Dermat. & Syph. **24**:1033 (Dec.) 1931.

the genera Monilia and Torula. The growth of these organisms was inhibited in dilutions of 1 : 1,000,000. Crystal violet, being a definite compound, was the best of the three violet dyes used. Other fungi tested withstood concentrations of the dye five times as strong.

2. Crystal violet showed curative value in the treatment of some dermatomycoses.

3. Other dyes, such as acid fuchsin, thionine, methylthionine chloride and eosin, seemed to stimulate in vitro the growth of fungi belonging to the fungi imperfecti, as well as strains of Saccharomyces, Trichophyton and Epidermophyton.

4. Mercurochrome showed no fungistatic action in dilutions of 1 : 500 but proved to be a powerful sensitizer to visible light. It inhibited the growth of strains Monilia, Saccharomyces, Epidermophyton and Trichophyton in dilutions of 1 : 10,000 after a short exposure to sunlight. Cure was obtained in one case of onychia and one of tinea after two treatments with mercurochrome plus irradiation with visible light for fifteen minutes.

5. Cresol was found to be very effective in its fungicidal action, killing the organisms in one-half minute when they were exposed to a 1 : 250 dilution. No other dilutions or shorter exposures were used

# KAPOSI'S VARICELLIFORM ERUPTION

## REPORT OF A CASE

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LOS ANGELES

In his textbook, Kaposi [1] called attention to an alarming complication of infantile eczema. He stated that the eruption looks like varicella but undoubtedly is not. It is accompanied with high fever, backache and other symptoms of varicella, but usually it does not cause prostration, although one child whom he observed died in convulsions. The distinctive feature of this eruption is its confinement to the upper part of the body of a person with an eczematous type of skin. Several years later, Juliusberg [2] described under the name "pustulosis varioliformis acuta" a disease picture which he subsequently recognized as the disease described by Kaposi. Since then, the condition has received little attention from dermatologists; it is either very rare or not often recognized. We were able to find only an additional twelve cases in the literature, although Kaposi stated in his original description that he had seen a total of ten. Until Brown [3] and McLachlan [4] recently published the histories of their cases, there had been none in the English or American literature. Although over a period of more than twenty-five years we have seen many patients with varioloid, variola and varicella, we cannot recall ever seeing a case of this type until recently. In a patient whom we had treated for eczema for approximately a year with good symptomatic improvement there suddenly developed an eruption accompanied by systemic symptoms such as Kaposi described.

### REPORT OF CASE

M. O., a woman aged 32, was first seen by us about a year ago. She had generalized eczema, which had been present for approximately four years. Under treatment, the skin condition improved appreciably. Then, suddenly, a definite

1. Kaposi, M. J.: Pathologie und Therapie der Hautkrankheiten, Vienna, Urban & Schwarzenberg, 1887, p. 483.

2. Juliusberg, J.: Ueber Pustulosis acuta varioliformis, Arch. f. Dermat. **45**: 21, 1898.

3. Brown, W. H.: Kaposi's Varicelliform Eruption, Brit. J. Dermat. **46**: 1 (Jan.) 1934.

4. McLachlan, A. D.: Kaposi's Varicelliform Eruption, Brit. J. Dermat. **46**: 8 (Jan.) 1934.

exacerbation of the eruption appeared on the face, neck, upper part of the chest and arms. We saw her about twenty-four hours after the first evidence of this eruption. There was definite edema of the whole face, including the eyelids, and less pronounced edema about the neck, chest and upper parts of the arms. There were no discrete lesions, and the palms or soles were not affected. The rest of the body was practically clear. In the area involved there was some distinct vesiculation. At that time the temperature was normal, but the cervical glands were large and tender. The eruption was confined largely to exposed areas. We suspected that it was an acute exacerbation of the eczema or a rhus dermatitis because the patient had been on the golf-links. In the next twenty-four hours there was little change except an aggravation of the symptoms. On the third day of observation there was a rise of temperature to 102 F.; the patient then complained of backache but was not prostrated. The eruption was about the same except that the edema had increased. On the fourth day it was apparent, especially on the arms, that the individual lesion was a papuloid vesicle. The systemic symptoms remained the same, but the temperature rose to 103 F. Except for the lack of appetite and the presence of the eruption, the patient had little complaint.

On the fifth day, we strongly began to suspect that the disease was variola. We could not make this diagnosis definitely because none of the lesions were characteristic. There were, however, a number of discrete lesions which when pricked readily oozed clear fluid. There was also a suggestion of delling of the lesions, but none were pustular. In the diffusely involved areas we gained the impression that the marked edema prevented the clearcut appearance of discrete lesions. Even on the fifth day, the eruption had not extended beyond the area originally involved, except for the development of possibly half a dozen lesions.

The temperature dropped to normal in twenty-four hours; from then on the lesions on the face discharged a serous material with considerable crusting. The rest of the lesions involuted rapidly with practically no discharge, and the adenopathy subsided with equal rapidity. At no time was there a typical varicella vesicle or variola pustule, but many lesions resembled these. The entire active course of the disease did not occupy more than eight days. However, the face now shows very superficial pitted scarring. The patient was vaccinated in infancy but not since. We could find no evidence of exposure to variola or varicella.

## COMMENT

Even in retrospect one could find nothing about the case that would permit a diagnosis of true varicella or variola. The lesions resembled varicella more than variola; apparently this is not characteristic of all cases previously reported. A diagnosis of varioloid or alastrim would have to be considered. It is possible that all these forms are related; if this is true, attempts at strict differentiation are futile. The course of the disease was too stormy and possibly too brief to be typical of varioloid, and the individual lesions were not characteristic. Kaposi's varicelliform eruption also seems to differ from alastrim; we have, however, had no personal experience with the latter. Descriptions of these diseases in textbooks vary, but a similarity cannot be denied. In this instance, while there were true vesicles, none of them arose from normal skin because edema was very pronounced. On the periphery there were some vesicles with distinct delling, but they never reached a pustular

stage. The mucous membranes were not involved, but the submental and cervical glands were enlarged and tender. The adenopathy was comparable to that seen in severe variola.

When Kaposi first described this eruption, he considered it distinctly a complication of infantile eczema. In his opinion it resembled varicella but was not that disease. He was inclined to look on it as an infection due to a yeast or possibly to a fungus in a skin left vulnerable as a result of eczema. All observers agree that Kaposi's eruption resembles vaccinia, varioloid, variola and varicella and that it is very difficult indeed to differentiate it from any of them. The two distinctive features of Kaposi's eruption are that eczema precedes it and that the eruption is confined to the upper part of the body throughout its entire course. Whether these features are sufficiently distinctive to classify it as a specific disease remains speculative. It is possible that a skin affected with eczema may have biologic characteristics capable of altering the virus of variola or varicella sufficiently to give it a specific clinical behavior. It was formerly assumed that the disease was confined to children, but McLachlan observed a case in a woman 25 years old. The case reported here also shows that it may occur in an adult. Osler frankly regards varioloid and alastrim as modified forms of variola, the result of previous vaccination, of some change in the virulency of the virus, or possibly of an inherited partial immunity. While such immunologic manifestations in the skin in addition to those of an allergic character may explain the peculiar behavior of Kaposi's eruption, even if it is the result of infection by the virus of variola, the clinical course is sufficiently distinctive and the diagnosis sufficiently puzzling to warrant cognizance of its existence. Either the disease picture is very rare in this country or no effort has been made to distinguish it from other varioliform or varicelliform eruptions.

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# AN EPIDEMIC OF RINGWORM DUE TO EPIDERMOPHYTON FLOCCOSUM (INGUINALE)

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Considerable attention has been given recently to epidemics and the incidence of ringworm of the toes and feet. Epidemics of ringworm of the scalp are also well known, while familial outbreaks of ringworm of the body are very frequent. One often hears reports that ringworm of the groins is prevalent in certain gymnasiums, but precise knowledge of such outbreaks seems lacking.

Sabouraud,[1] in his textbook, described an epidemic of ringworm of the groins which occurred in a Parisian college in 1906 and which involved twenty-three men. He also referred to several different outbreaks of the infection, among them one described by Dubreuilh in 1894, in which twenty young men were affected. From his patients Sabouraud isolated a fungus to which he gave the name Epidermophyton inguinale. Castellani, working independently at that time, named the organism Trichophyton cruris.

It is of interest to note that several years previously, in 1870, Harz had isolated the fungus from epidermal scales in cases of eczema marginatum (ringworm of the groins). He described its exact morphology and cultural characteristics, made drawings and designated the organism Acrothecium floccosum. Langeron and Milochevitch,[2] in 1930, pointed out that the correct name of this fungus is Epidermophyton floccosum. This view has also been taken by Ota [3] and Emmons [4] in more recent publications.

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From the Departments of Dermatology and the DeLamar Institute of Public Health, College of Physicians and Surgeons, Columbia University.

1. Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910, p. 420.

2. Langeron, M., and Milochevitch, S.: Morphologie des dermatophytes sur milieux naturels et milieux à base de polysaccharides. Essai de classification, Ann. de parasitol. **8**:465, 1930.

3. Ota, M.: Epidermophyton-Epidermidophyton, Ann. de parasitol. **9**:277, 1931.

4. Emmons, C. W.: Dermatophytes, Arch. Dermat. & Syph. **30**:337 (Sept.) 1934.

Guy and Jacob [5] studied thirty-five cases of Tinea circinata of the arm which followed vaccination and reported that at least some cases were due to E. floccosum (inguinale). Ten patients of their group also showed lesions of the feet. At one time there was a tendency to ascribe all ringworm of the hands and feet to this fungus, though Mitchell [6] refuted this in part by showing that in a series of seventeen such cases only six were caused by E. floccosum (inguinale). In the extensive investigations for ringworm among the first year students at the University of California, Legge, Bonar and Templeton [7] reported that of six hundred and thirty-five cases in which the tests were positive seventy-seven were due to E. floccosum (inguinale). Among the men infected 9.3 per cent showed evidence of crural ringworm.

Thus the frequency of infection by E. floccosum has been recognized, and several epidemics have been observed.

This report concerns an outbreak of infections with this fungus that occurred among the crew of four hundred men on a large steamship. The vessel was modern in construction and devoted mainly to passenger service, making frequent sailings from New York.

The first two cases occurred in August; one month later there were four cases, and in the following month, twenty-six cases. On each arrival in New York the men known to be infected were sent to a hospital for isolation and were cared for at the company's expense. By this time the spread of this relatively harmless infection had become alarming, and the costs to the shipping company were mounting. Although no cases were known to have occurred among the passengers, the danger of this could not be ignored.

This study was made in an effort to determine the cause of the epidemic and to check its spread.

## CHARACTER OF THE EPIDEMIC

From the history of the epidemic no explanation of its origin could be obtained. The general sanitary regulations of the ship seemed adequate. No mascots or pets were kept by the crew. Suspicion had attached to a swimming pool frequently used by the crew at a foreign port of call; this had been closed, however, for over a month, and new cases continued to occur. Moreover, no cases were known to have occurred among landsmen using the pool. The striking point was that

5. Guy, W. H., and Jacob, F. M.: Epidermophytosis: A Sequel to Vaccination, Arch. Dermat. & Syph. **12**:233 (Aug.) 1925.

6. Mitchell, J. H.: Further Studies on Ringworm of the Hands and Feet, Arch. Dermat. & Syph. **5**:174 (Feb.) 1922.

7. Legge, R. T.; Bonar, L., and Templeton, H. I.: Epidermomycosis at the University of California, Arch. Dermat. & Syph. **27**:12 (Jan.) 1933.

the only known cases were among the stewards, the deck and engine-room hands remaining free. All of this pointed to direct or indirect transmission on board.

### INSPECTION OF THE SHIP

An inspection was made of the ship while it was in port. The quarters for most of the stewards were on the D and E decks forward, separated from those of the other hands. Visiting between quarters was not, however, prohibited. One laundry man quartered aft among the deck hands was among the first to become infected; two others sharing his compartment were later found to be infected.

The compartments accommodated from two to eight men. Showers and toilets adjoined the cabins. The floors were of steel and painted concrete. The ship's laundry washed only bed linen and towels; the laundering and the dispensing of the linens were efficient. Each man cared for his personal articles at various laundries ashore or washed them in common tubs aboard ship.

The only striking defects were the allowance of only one medium-sized towel a week for each man and the disorder in their quarters while in port. Towels, underwear and other clothing were scattered over bunks, floors and stools.

### INSPECTION OF THE CREW

One of us (S. T. M.) made the next voyage in order to inspect the crew. About three hundred men, stripped, were examined individually with the cooperation of the ship's doctor. The circumstances made the examination of the feet difficult, and this was done only in cases in which the patient showed lesions elsewhere. Microscopic examinations and cultures were made of material from a few persons with typical lesions and from a number suspected of having the condition. The examination of most of the men was repeated from three to six days later on the return voyage.

Eighteen men were discovered to have typical cases and immediately placed under treatment. One man worked in the engine-room, and one was a hospital attendant, which showed that the epidemic, though chiefly among the stewards, was not confined to them. The patients held in the hospital in New York were also examined by one of us (G. J. F.). Two more cases occurred a few weeks later, after the completion of the voyage, making a total of fifty-two known cases. The distribution of the lesions in these cases is shown in table 1.

Many of the men showed batwing-shaped, red, finely scaling plaques in the groins typical of tinea cruris. Others showed small circinate patches, often only in the axillae. Nearly half of the patients had

intertrigo of the toes; in a few instances it was severe, while in others it was moderate. The most interesting feature was that five patients showed a widely disseminated eruption on the trunk and extremities. In these cases and in some of the cases of inguinal localization the lesions were edematous, weeping and unusually painful. While this may have been due to irritating treatment, it suggested an infection of exceptional virulence.

Several men with typical ringworm of the groins also showed reddish scaling areas on the arms and body in which no fungus could be found and which may have been epidermophytids. In addition to the tabulated cases there were seven questionable cases in which the condition simulated tinea cruris but in which microscopic examination and cultures showed no organisms. The lesions in these cases gradually subsided without treatment. A few other men showed red, nonscaling

TABLE 1.—*Distribution of the Lesions*

| Area | Number of Cases | Number of Cases Accompanied by Lesions of the Toes |
|---|---|---|
| Groins and adjoining surfaces | 22 | 11 |
| Groins and axillae | 9 | 4 |
| Groins and neck | 2 | .. |
| Generalized (trunk, extremities, groins) | 5 | 4 |
| Axillae | 11 | 4 |
| Buttocks | 1 | 1 |
| Scrotum | 1 | .. |
| Pubic region | 1 | .. |
| Total | 52 | 24 |

patches in the groins which, though they had not been treated, resembled healed lesions of tinea.

The following cases are illustrative:

## REPORT OF CASES

CASE 1.—H., a bedroom steward, aged 45, had his quarters, toilet and showers on D deck. His laundry was done ashore, except his socks, which he washed himself.

After he had been swimming one week previously a widespread eruption consisting of well circumscribed erythematous lesions appeared on the groins, axillae, chest, thighs, gluteal folds, arms and legs. The lesions soon became confluent in many places. The toes showed maceration. The patient was isolated and treated ashore for six weeks and then returned to the ship as recovered. Eleven days later new lesions developed in the axillae. It may be noteworthy that the patient was again wearing an elastic stocking when he returned to work. It had been discarded for six weeks during his stay in the hospital. This fact may have had some bearing on the prompt recurrence of the infection.

CASE 2.—W., aged 16 years, a page boy, had his quarters, toilet and showers on D deck. All his personal laundry was done ashore. One of his four cabin

mates had previously been infected. The patient had been swimming in the pool five weeks previously. Examination showed circumscribed patches in the crural region and on both sides of the neck. The lesions consisted of erythema, vesicles and some scaling; their margins were slightly raised. The toes were normal. Mycelia were observed in the lesions on the neck and groins. Cultures of material from the neck and groins produced colonies of E. floccosum.

CASE 3.—R., a printer, had his quarters, toilet and showers on E deck. He had one infected cabin mate; he did not use the pool. Examination revealed raw erythematous circinate lesions on the groins and thighs. The toes showed maceration of the interdigital spaces. Examination revealed mycelia in the lesions of the groins and toes. Cultures of material from the groins and toes produced colonies of E. floccosum.

That a crew of this size on a sea-going vessel can furnish some interesting dermatologic material is well proved by the many other

TABLE 2.—*Diseases Other Than Ringworm Observed in the Crew*

| Disease | Number of Cases |
|---|---|
| Erythrasma | 3 |
| Tinea versicolor | 2 |
| Pityriasis rosea with a herald patch (also tinea of the feet, as evidenced by slide) | 1 |
| Pediculosis pubis (one case associated with folliculitis due to mercury) | 2 |
| Psoriasis of the scalp and body | 1 |
| Syphilis—a generalized secondary eruption | 1 |
| Seborrheic dermatitis of the scalp, back and chest | 1 |
| Folliculitis of the axillae (this may have been secondary to tinea) | 1 |
| Impetigo of the face (patient also had tinea of the groins) | 1 |
| Urticaria (patient also had tinea of the groins) | 1 |
| Tuberculosis verrucosa cutis of the buttocks (there was a family history of tuberculosis) | 1 |

conditions that were found during the general inspection. In addition to the cases of ringworm the diseases listed in table 2 were present.

## MYCOLOGIC EXAMINATIONS

A thorough mycologic survey was impracticable. Slides prepared from material from seventeen patients with clinically typical cases showed mycelia in eight instances. Five positive cultures were obtained from typical lesions in five cases: in two with material from the groin, in one, from the axilla, in one, from the neck, and in one, from the feet. All the colonies were typical of E. floccosum (inguinale). On Sabouraud's maltose agar they formed a flattened cone with an irregularly cupped eccentric apex and radial folds extending to the fringed borders. The surface was powdery and greenish yellow. Microscopically they showed numerous egg-shaped or club-shaped septate macroconidia (*fuseaux*) singly or in clusters. There were no conidia, but some cultures contained numerous chlamydospores.

This evidence indicates that the epidemic was due to this fungus. E. floccosum is a frequent cause of epidermophytosis of the groins, axillae and toes. It rarely invades other areas, and in the past four years at the Vanderbilt Clinic only three cases were seen in which other locations were involved. The postvaccinal lesions described by Guy and Jacob occurred on the arm and elsewhere; Weidman [8] cited two cases of generalized eruption from France, and nine were reported from Germany by Fischer.[9] Fischer gave no description of the cultures obtained in his cases, although he called the fungus E. inguinale.

E. floccosum usually seems to be of low virulence. Inoculation of animals has been unsuccessful. Bruhns and Alexander [10] stated that inoculation of man usually fails unless the skin is macerated with wet dressings. It is of interest that in some of these cases some lesions were widespread and highly inflammatory.

As the possibility of transmission by baths was considered, tests were made of the viability of this fungus. Fragments of old dried cultures were suspended in filtered sterilized sea water and also in soap solutions and after eleven weeks they showed evidence of growth in this medium. Subcultures yielded typical colonies.

## MODE OF CONTAGION

From these examinations it was impossible to pass final judgment as to the mode of contagion, but two facts stood out. One was that the isolation of only those men who voluntarily reported for treatment accomplished nothing, as an inspection of the crew revealed eighteen other patients by which the epidemic could be carried.

The other was that infection probably occurred through the interchange of towels, blankets and clothing in the sleeping quarters. There were eighteen compartments in which from two to four cases occurred, and the disorder was such that the men could not be sure that they were using their own towels.

Whether infection occurred from shower-baths or toilet seats was difficult to determine. We could not make certain whether or not cross-infection was common among men using the same baths. The question is further obscured by the difficulty in evaluating the infections of the feet. Infection from a shower-bath should occur first on the feet. Over half the men had no lesions on the feet, and in these cases the baths

8. Weidman, F. D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

9. Fischer, W.: Ueber die generalisierte Form des Ekzema marginatum, Berl. klin. Wchnschr. **52**:241, 1915.

10. Bruhns, C., and Alexander, A., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11, 208.

could hardly have been responsible. In the others there was a question as to whether the lesions on the feet were a part of the present epidemic. In the patient from which E. floccosum was isolated they probably were, but in others the infection of the feet may have been a matter of long standing and due to some other fungus.

Any outside source of infection seemed excluded. It seemed that we were dealing with an infection transmitted from patients with concealed cases, chiefly by interchange of towels or blankets in the sleeping compartments but possibly also by the floors in the showers and the toilet seats.

## PREVENTION OF CONTAGION

On the basis of these observations the following procedures were recommended roughly, in order of their importance:

1. Examination of the entire crew once a week; immediate treatment and isolation when possible.

2. Daily inspection of the sleeping quarters and maintenance of order.

3. Issuing of towels three times a week.

4. Disinfection of blankets and mattress covers.

5. Scrubbing of bathrooms and toilet seats with a 2 per cent solution of cresol.

6. Provision of foot-tubs containing 1 per cent sodium hypochlorite solution (renewed daily) in washrooms adjoining the showers.

As noted earlier, two cases developed on the next voyage, and we have been informed that occasional cases have occurred since but that the problem is no longer serious. In general, the aforementioned measures seemed effective.

## SUMMARY

An epidemic of crural ringworm among the crew of a passenger liner is reported. It involved fifty-two men.

Infection apparently occurred in the sleeping quarters and was kept going by the presence of undetected cases among the crew.

The severity of some of the cases was notable. Five men presented generalized lesions, while several others showed indefinite lesions suggestive of epidermophytids.

All the cultures obtained were typical of E. floccosum (inguinale).

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# EFFECT OF THE ROENTGEN RAYS ON THE LIPIDS OF THE EPIDERMIS

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As nothing definitely has been proved to explain biologically the effect of roentgen rays on the human skin, it was decided to begin in this field of many theories by studying quantitatively, and as accurately as possible, the effect of the roentgen rays on the lipids of the human epidermis.

One fact that makes such a study logical is the striking reduction in the lipid content of carcinomatous tissue after roentgen therapy. Also, the findings of other observers on the blood cholesterol content following roentgen therapy have been rather startling. Malczyński [1] noted a considerable rise of blood cholesterol during the two weeks following irradiation of areas of skin on the backs of dogs with either the ordinary roentgen rays or with the Grenz rays. Mader and Bingenheimer [2] found that roentgen irradiation of mongolian idiots, whose blood cholesterol is low, as a rule, produces a rise in blood cholesterol to a value several times that of the pretreatment reading.

## METHOD OF STUDY

Samples of epidermis were obtained from the soles of chilled, unembalmed cadavers on the autopsy table a few hours after death by paring with a sharp, straight edged razor, care being taken not to include the corium. It was thought that specimens from the soles would be more likely to give data on the intrinsic epidermal cell lipids than scrapings from the glabrous skin, in which the sebum present might interfere with the study.

In each instance the specimen was divided into two parts. One part was weighed accurately and kept as a control (A). The other (B) was weighed accurately, irradiated with 900 roentgen units of unfiltered radiation (120 kilovolts, 30 cm., 5 milliamperes, 9 minutes). During the irradiation the parings were spread on glass to a depth of not over 3 mm.

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Studies and Contributions from the Department of Dermatology and Syphilology and the Department of Physiological Chemistry of the University of Michigan Medical School.

1. Malczyński, S.: Compt. rend. Soc. de biol. **111**:315 (Oct. 31) 1932.
2. Mader, A., and Bingenheimer, E.: Jahrb. f. Kinderh. **138**:9, 1933.

Henceforth both the control (A) and the irradiated portion (B) were treated and analyzed alike. The total lipids in the tissues were removed by means of cold extractions with various fat solvents. This method of cold extraction seemed desirable because of the fact that heat is known to alter some of the constituents of the total lipids. The process of extraction consisted of immersion of the tissues in 95 per cent ethyl alcohol for a period of forty-eight hours and extraction with absolute alcohol for a similar length of time, then with anhydrous ethyl ether and finally with chloroform. The combined extracts were concentrated to a small volume in vacuo at a low temperature. The resulting fluid was taken up in petroleum ether and washed thoroughly with water, and after removal of the petroleum ether by distillation it was dissolved in chloroform and made up to a definite volume. The total lipids were determined by evaporating the solvent from an aliquot of the solution and weighing the solids thus obtained. The cholesterol was determined colorimetrically with the Liebermann-Burchard test, and the phospholipids were estimated by means of a procedure outlined by Whitehorn.

TABLE 1.—*Effect of Roentgen Radiation on Some of the Lipid Constituents in the Human Epidermis*

| | Weight of Sample, Gm. | | Weight of Total Lipids, Mg. | | Percentage of Lipids, in Sample | | Percentage of Cholesterol in Sample | | Percentage of Cholesterol in Total Lipids | | Percentage of Phospholipids in Sample | | Percentage of Phospholipids in Total Lipids | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample | A | B | A | B | A | B | A | B | A | B | A | B | A | B |
| 1 | 0.9935 | 1.123 | 28.8 | 14.8 | 2.9 | 1.3 | 0.8 | 0.75 | 27.7 | 56.9 | | | | |
| 2 | 0.865 | 0.920 | 18.4 | 20.0 | 2.13 | 2.17 | 0.83 | 0.84 | 39.0 | 38.5 | | | | |
| 3 | 1.952 | 2.382 | 36.0 | 36.0 | 1.84 | 1.51 | 0.58 | 0.46 | 32.0 | 30.7 | 0.036 | 0.020 | 1.9 | 1.3 |
| 4 | 1.941 | 1.221 | 40.0 | 22.4 | 2.06 | 1.8 | 0.603 | 0.636 | .... | .... | 0.026 | 0.0125 | 1.29 | 0.7 |
| 5–6 | 4.12 | 4.145 | 46.0 | 40.0 | 1.12 | 0.96 | 0.54 | 0.42 | 48.9 | 44.4 | 0.032 | 0.0201 | 2.894 | 2.082 |
| 7–8 | 4.59 | 3.49 | 52.0 | 40.8 | 1.11 | 1.13 | 0.63 | 0.61 | 55.9 | 53.3 | | | | |
| 12 | 12.25 | 11.76 | 165.0 | 107.0 | 1.35 | 0.91 | 0.39 | 0.33 | 29.1 | 36.5 | 0.080 | 0.044 | 6.7 | 4.8 |

## RESULTS

The data in table 1 summarize the results which were obtained. The letter A in that summation designates that the data in that column are for controls (i. e., unirradiated material); the letter B indicates that the data are for specimens which were subjected to the action of roentgen rays. In five of the seven samples reported on in table 1 a loss in total lipids occurred when the tissues were exposed to the roentgen rays. The investigation made of sample 1 was merely explorative. Owing to the paucity of the material, only the total lipids and total cholesterol were determined. In this instance it was apparent that exposure to the roentgen rays resulted in a considerable loss of lipids. Sample 2 likewise was studied superficially; no demonstrable alteration could be shown. For the other samples more information was secured, for it was possible to determine not only total lipids and cholesterol but also total phospholipids. The results obtained show that in every instance a loss of phospholipids took place. The losses which are shown in table 2 are calculated on the basis of the original phospholipid and cholesterol content of the control tissue.

These tables indicate that whenever the epidermal tissue was exposed to roentgen rays an appreciable loss of phospholipids took place and that in the major portion of the cases studied a smaller but determinable loss of cholesterol was likewise apparent.

From what has been discussed thus far one might conclude that irradiation causes a loss of total lipids, usually a loss of cholesterol and always a loss of phospholipids. (The predominating loss of the substances determined is in the phospholipids.) However, after examining the data further, one may arrive at a different conclusion. In order to call attention to this change in the point of view, we have calculated our

TABLE 2.—*Losses Calculated on the Basis of the Original Phospholipid and Cholesterol Content of the Control Tissue*

| Sample | Cholesterol Loss, Percentage | Phospholipid Loss, Percentage |
|---|---|---|
| 1 | 6.25 | .... |
| 2 | None | .... |
| 3 | 20.7 | 33.3 |
| 4 | None | 50.0 |
| 5-6 | 22.2 | 37.5 |
| 7-8 | 3.1 | .... |
| 12 | 15.4 | 45.0 |

TABLE 3.—*Actual Losses of Total Lipids, of Total Cholesterol and of Total Phospholipids*

| Sample | Loss in Total Lipids, Gm. per 100 Gm. of Tissue | Loss Due to Cholesterol, Gm. per 100 Gm. of Tissue | Loss Due to Phospholipids, Gm. per 100 Gm. of Tissue |
|---|---|---|---|
| 1 | 1.6 | 0.05 | ..... |
| 2 | None | None | ..... |
| 3 | 0.33 | 0.12 | 0.016 |
| 4 | 0.26 | None | 0.013 |
| 5 | 0.16 | 0.12 | 0.012 |
| 12 | 0.44 | 0.06 | 0.036 |

data in a different manner. Table 3 shows the actual losses of total lipids, of total cholesterol and of total phospholipids per hundred grams of tissue. On examining these data, one finds that most of the loss in total lipids took place not at the expense of phospholipids but at the cost of the cholesterol. Our data indicate, therefore, that not only the phospholipids but the sterols may be altered readily by the application of roentgen rays.

## TECHNICAL COMMENT

The data on the phospholipids are probably more accurate than those on the cholesterol because the method employed for the determination of phospholipids is more reliable than that used for the determination of cholesterol. In the determination of phospholipids the lipids are all oxidized with strong nitric acid to destroy products

which in the end might produce an interfering color in the colorimetric determination. In the determination of cholesterol, however, certain substances are present in the total lipids which give a yellow color with the reagent employed. Thus when one attempts to compare the color of the sample under analysis with that formed from the pure cholesterol standard, one is confronted with the difficulty of matching solutions which differ in color. We do not believe, however, that this fact can account entirely for the results obtained. If we had had enough material available, we should have determined the cholesterol content of the tissues by means of the digitonin method as this is a gravimetric procedure which gives more reliable data.

In addition, if it had been possible to irradiate the epidermis of a living person and then obtain specimens for analysis, our results might have been more accurate. However, as the stratum corneum of the sole is made up largely of dead cells, it is felt that this difficulty has been at least partially avoided.

## CONCLUSION

The results of this study indicate that the roentgen rays tend to produce a reduction of the total lipids of the human epidermis and that at least the cholesterol and the phospholipids participate in this reduction.

# ESSENTIAL SYPHILITIC ALOPECIA

## REPORT OF A CASE

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In 1925, Wile and Belote [1] called attention to the subject of alopecia in syphilis and gave an excellent summary of it, emphasizing the important contributions of Cyranka and of Gartner and discussing the two types of syphilitic alopecia: (1) essential alopecia, the type which occurs without visible accompanying syphilids in the scalp; (2) symptomatic alopecia, the type in which the loss of hair is apparently due to lesions of syphilis in the scalp.

The first type, essential alopecia, is less understood. It is of interest in this discussion because the case under consideration helps to confirm the findings of Wile and Belote, who stated (1) that essential syphilitic alopecia is frequently associated with meningeal syphilis and (2) that the loss of hair is most likely due to an endocrine dysfunction resultant from a syphilitic lesion in the sympathetic ganglions.

A case most striking in its clinical aspect and emphasizing these points has come under my observation.

### REPORT OF A CASE

Mrs. A. S., a 39 year old American housewife, consulted me on account of a generalized falling of hair of two months' duration. Except that she had been nervous for several years, she had no subjective symptoms. Examination of the scalp revealed nothing of importance; it was clean and loose. By running the hands through the hair, one could remove about forty long hairs without traction. The hair shafts were thick and appeared normal under magnification. There were no bald patches. The patient had a thick growth of long hair which showed no thinning in spite of the loss of hair for a period of two months.

The findings of the general examination were as follows: (1) widening of the palpebral fissures; (2) a prethyroid erythema beginning as a slight blush, punctate and becoming dusky and intensely red as the examination proceeded; (3) a noticeable fulness of the thyroid gland, which was palpable; (4) a fine tremor of the hands and tongue; (5) a pulse rate of 76; (6) a blood pressure of 150 systolic and 90 diastolic; (7) two infected teeth; (8) palpable lymph nodes in the cervical region; (9) exaggerated knee jerks; (10) slight swaying (a questionable Romberg sign) and (11) all other reflexes, superficial and deep, normal. These signs suggested hyperthyroidism and possibly cerebrospinal syphilis. Laboratory examination showed: basal metabolic rate, +29; Wassermann, Kahn and Hinton blood

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From the Pittsburgh Skin and Cancer Foundation.

1. Wile, Udo J., and Belote, George H.: Syphilitic Alopecia: Its Relation to Neurosyphilis, Arch. Dermat. & Syph. **13**:495 (April) 1926.

tests, strongly positive. Examination of the spinal fluid revealed: cell count, 285 per cubic millimeter; Wassermann test, strongly positive.

Reinquiry of the patient regarding syphilis revealed only that she had been married four years and had not become pregnant in spite of the fact that no contraceptives were used. Examination of the husband showed him to be free from any physical or serologic evidence of syphilis.

With antisyphilitic therapy, the fall of hair stopped, and the nervousness and tremor of hands and tongue lessened greatly. The patient is feeling much better.

I believe this to be a highly instructive case and definitely corroborative of the contention of Wile and Belote that essential syphilitic alopecia results from the effect of the autonomic nervous system on a specific ductless gland; in this instance the thyroid gland was involved.

# EPITHELIOMA ADENOIDES CYSTICUM WITH FEATURES OF SYRINGOMA

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Epithelioma adenoides cysticum (Brooke [1]), tricho-epithelioma (Jarisch [2]), adenoma sebaceum (Pringle [3]) and syringoma (Jacquet and Darier [4]) are usually described as separate entities. This report is of a case which clinically and histopathologically fulfilled the requirements for a diagnosis of any of these diseases and which afforded evidence to regard them as manifestations of the same disease. Cylindroma belongs in the same group, as Watanabe [5] and Stillians [6] have shown.

The literature regarding epithelioma adenoides cysticum, tricho-epithelioma, adenoma sebaceum, syringoma (syringocystadenoma or *hydradénomes éruptifs*), not to speak of adenoma of the sebaceous glands and cylindroma (nevus epithelioma cylindromatosis), is large and confusing. There is a multiplicity of names for each of the conditions just mentioned. Furthermore, a critical analysis of many cases revealed the histopathologic features of more than one condition and a disagreement in interpretation of similar pathologic findings. The pertinent literature was given by Summerill and Hutton; [7] that for cylindroma was given by Stillians. Complete references were given by Beck.[8]

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Abstract of a thesis submitted in 1933 to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. Brooke, H. G.: Epithelioma Adenoides Cysticum, Brit. J. Dermat. **4**:269 (Sept.) 1892.

2. Jarisch: Zur Lehre von den Hautgeschwülsten, Arch. f. Dermat. u. Syph. **28**:163, 1894.

3. Pringle, J. J.: Ueber einen Fall von kongenitalem Adenoma sebaceum, Monatsh. f. prakt. Dermat. **10**:197, 1890.

4. Jacquet and Darier: Hydradénomes éruptifs, Ann. de dermat. et syph. **18**:317, 1887.

5. Watanabe, Jujiro: Ueber das Cylindrom und das Epithelioma Adenoides Cysticum, Arch. f. Dermat. u. Syph. **140**:208, 1922.

6. Stillians, A. W.: Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **27**:481 (March) 1933.

7. Summerill, Frederick, and Hutton, J. G.: Multiple Benign Cystic Epithelioma (Epithelioma Adenoides Cysticum) with Summary of Literature, Arch. Dermat. & Syph. **26**:854 (Nov.) 1932.

8. Beck, S. C.: Epitheliome, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, p. 208.

From careful analysis of the cases in the literature I wish to give the following brief summary: Epithelioma adenoides cysticum, tricho-epithelioma and adenoma sebaceum are so closely related as to be indistinguishable clinically or pathologically. Syringoma differs from the group of conditions known under the designation of epithelioma adenoides cysticum in that no hereditary factor is reported and the lesions tend to be somewhat smaller. Gans [9] emphasized that histologically the epidermis usually is not involved. The cysts and epithelial strands have been traced to the sweat ducts but not to well developed sweat glands. Csillag,[10] Neumann [11] and Philippson,[12] however, reported cases in which there were acanthosis of the epidermis and involvement of the rete ridges. Weidman and Besançon [13] and McDonagh [14] cited cases in which epithelioma adenoides cysticum and syringoma were present in the same patient, although occurring apparently in separate lesions. It is my belief that Brooke's and Hartzell's [15] cases and other cases presented features of both diseases in the same section. Cylindroma (nevus epithelioma cylindromatosis) usually can be distinguished from the foregoing clinically by the larger and more variable size of the lesions, with their predilection for occurring in the scalp and histologically by the characteristic hyaline change about and within the nests of epithelial cells, representing hyaline changes in the connective tissue or in the epithelial cells themselves. In some cases, however, pathologic features of both epithelioma adenoides cysticum and cylindroma are present (Watanabe and Stillians). Adenoma sebaceum (Pringle) has no relation to the condition known by the terms sebaceous gland adenoma, nevus sebaceus (Gans [16]) and

9. Gans, Oscar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 255.

10. Csillag, J.: Ueber das Syringom, Arch. f. Dermat. u. Syph. **72**:175, 1904.

11. Neumann, J.: Das Syringocystom, Arch. f. Dermat. u. Syph. **54**:3, 1900.

12. Philippson, L.: Die Beziehungen des Colloid-Milium (E. Wagner) der colloiden Degeneration der Cutis (Besnier) und des Hydradenoms (Darier-Jacquet) zu einander, Monatsh. f. prakt. Dermat. **11**:1, 1890.

13. Weidman, F. D., and Besançon, J. H.: Histologic Differences in a "Syringoma" of the Face and Shoulder: Employment of Wax Reconstruction, Arch. Dermat. & Syph. **21**:279 (Feb.) 1930.

14. McDonagh, J. E. R.: Case of a Mixed Tumor (Tricho-Epithelioma Papulosum and Syringocystadenoma, Proc. Roy. Soc. Med. (Dermat. Sect.) **3**:32 (Dec. 16) 1910.

15. Hartzell, M. B.: Benign Cystic Epithelioma and Its Relationship to So-Called Syringocystadenoma, Syringocystoma and Haemangio-Endothelioma, Brit. J. Dermat. **16**:361, 1904; A Further Contribution to the Study of Benign Cystic Epithelioma, J. M. Research **18**:159, 1908.

16. Gans, Oscar: Ueber Syringom; ein Beitrag zu ihrer Genese und Systematik, Arch. f. Dermat. u. Syph. **141**:232, 1922.

senile sebaceous adenoma (Nomland [17]). Clinically, in the latter condition, the lesions are yellow, soft and irregular in shape; histologically, they have to do only with hypertrophy or proliferation of the sebaceous glands. Reference must also be made to the occasional association of any of the foregoing conditions with vascular nevi or with true nevus cells.

Summerill and Hutton presented an interesting clinical differential table regarding the diseases just mentioned and also regarding solitary adenomas of sweat glands and basal cell epitheliomas; they admitted that biopsy usually is necessary for diagnosis and classification. The clinical or histopathologic differentiation from basal cell epitheliomas should offer no difficulty for the dermatologist or dermatohistopathologist, admitting that, as the result of trauma or of chronic irritation, any of the foregoing conditions may eventuate in basal cell epitheliomas or carcinomas. A review of the literature, however, shows that this is an exceedingly rare occurrence.

## ETIOLOGY

Epithelioma adenoides cysticum has been regarded by many investigators as tricho-epithelioma because of the presence of sebaceous cells and deposits of melanin. The latter, however, is characteristic of involvement of the epidermis as well as of the hair follicles. The interpretation of epithelioma adenoides cysticum as syringoma does not explain the presence of sebaceous cells or of hyperplastic hair follicles. That the strands of epithelial cells resembling sweat ducts cannot in either condition be demonstrated as arising from mature sweat glands simply means that the pathologic process has not extended deeply enough. In the case which I am presenting I have shown that the connection with the sweat ducts and with the hair follicles is near, or in, the epidermis. This, however, need not imply a true metaplasia, as was encountered in Walther and Montgomery's [18] case of solitary, verrucous lesion of the palm in which a benign tumor resembling a sweat gland gave evidence of epithelial metaplasia toward a structure similar to that of a mucous gland. Rather, the closer the sweat ducts approach the epidermis, the more involved they are in hyperplasia. If one accepts Krompecher's [19] views regarding the basal cell origin of benign or malignant tumors, not only from the epidermis, but also from the dermal appendages, including

17. Nomland, Ruben: Senile Sebaceous Adenoma, Arch. Dermat. & Syph. **22:** 1004 (Dec.) 1930.

18. Walther, Max, and Montgomery, Hamilton: Schweissdrüsentumor mit Epithelmetaplasie, Arch. f. Dermat. u. Syph. **163:**420, 1931.

19. Krompecher, E.: Zur Kenntnis der Geschwülste und Hypertrophien der Schweissdrüsen, Arch. f. Dermat. u. Syph. **126:**765, 1919; Zur vergleichenden Histologie der Basaliome, Ztschr. f. Krebsforsch. **19:**1, 1922.

the hair follicles, sweat glands and sebaceous glands, a definite relationship is apparent. Kyrle [20] explained the failure of the cells of the basal cell epithelioma to differentiate and become keratinized, as normal basal cells do, on the basis that the basal cell layer of the epidermis has two tasks: (1) to differentiate into pavement epithelium and (2) to act as the matrix for the postfetal formation of glands. In discussing Stillians' article, Weidman [21] pointed out that three kinds of tumors of the skin can be derived from a common embryonic structure, namely, the skin plate of Remak, which at first is not sweat duct, epidermis or hair follicle. Kyrle explained syringoma on the basis of the formation of an aberrant, apocrine gland. The term "nevus," as applied to this case or to the other conditions referred to, probably has been justly criticized by Scholtz, and it should not be used.

## REPORT OF A CASE

A man of Scotch descent, a bachelor, aged 40, who owned a "rent-a-car" business and formerly had been a military instructor, first came to the Mayo Clinic in 1931 because of skin trouble which had started around the eyes four years previously. The condition had gradually caused ectropion, the eyes becoming sore and discharging matter. The orbital fissures had become markedly narrow, subsequently interfering with vision (fig. 1). The eyelashes had gradually disappeared a year later. The cornea had never been affected. A diagnosis of trachoma had been made. Nine months before admission, the patient had noticed milium-like lesions on the rest of the face, and the skin had become red and stiff. At the same time a nevus-like, red-brown, finely papular plaque had appeared on the back. Four months later, lesions had appeared on the first phalanges of the fingers. Then the rest of the body apparently had gradually become involved, except the palms and the soles.

The patient had complained of a feeling of lassitude for two or three years previously and, at about the time of the first admission, of a decrease in sexual desire. Six years previously he had noticed a small mass in the right breast close to the nipple and soon afterward one in the left breast, which had gradually increased in size. There had been no change in weight or in sweating. There was no history of a similar skin disease in the family.

General examination gave essentially negative results. The basal metabolic rate was —3 per cent; the systolic blood pressure was 96 mm. of mercury, and the diastolic, 62 mm. The tonsils were moderately infected. Lymph nodes in the left and right axillae were scarcely palpable. The blood picture was normal; the value for urea was 22 mg. per hundred cubic centimeters of blood.

Dermatologic examination revealed marked involvement of the face, the upper portion of the back, the thorax and the extremities, although lesions were present over the entire body except the palms, soles and scalp. The elementary lesions seemed to be follicular papules, glassy translucent cysts or tissue which had undergone hyperkeratosis, with a feeling similar to that of a nutmeg-grater. The

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20. Kyrle, Joseph: Beitrag zur Frage der Basalzellengeschwülste der Haut, Arch. f. Dermat. u. Syph. **121**:246, 1915.

21. Weidman, F. D., in discussion on Stillians, A. W.: Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **27**:489 (Feb.) 1933.

cysts when opened exuded globular, smooth bodies on being squeezed. The skin was somewhat reddened and hyperemic, with a faint brownish tinge. The face had a masklike appearance; the nose was not involved. Ectropion and narrowing of the orbital fissures, alopecia of the eyelashes and partial alopecia of the eyebrows and of the hair in the axillary and pubic regions were present. The changes in the skin as a whole were suggestive of pityriasis rubra pilaris, the more so because the first phalanges of the fingers and the toes revealed the characteristic follicular lesions. One plaque on the back, 5 cm. in diameter, had a nevoid appearance; it was deep red and composed of thickly set, milium-like papules.

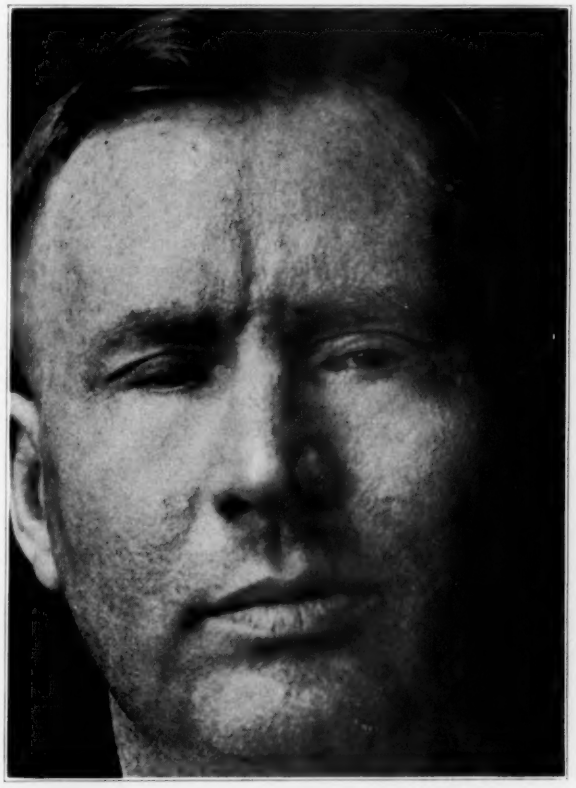

Fig. 1.—The face is studded with small lesions, giving it a rough appearance. The folds are ironed out, the orbital fissures are narrowed, and ectropion is present. The tip of the nose is free from lesions.

The patient was admitted to the hospital for observation and treatment. Sweating was induced by administering ⅛ grain (0.008 Gm.) of pilocarpine three times a week. Desiccated thyroid substance was given three times a day, and colloid baths daily. A sample of sweat induced by pilocarpine was procured; on analysis it revealed 34 mg. of urea, 20 mg. of chlorides, 22.6 mg. of nonproteins and 0.8 mg. of total proteins per hundred cubic centimeters. Clinically, the patient had improved considerably, the skin having become more pliable and soft. Two years

later, in 1933, it was reported in a letter that there was increasing ectropion, which interfered with vision, and that the patient had difficulty also in opening his mouth.

Specimens for biopsy were taken from the back and the finger on admission in 1931 and again three weeks later. More than four hundred serial sections were studied, and wax reconstructions were made from two areas (figs. 2 to 5). The section of skin taken from the nevoid plaque on the back presented the following features: The epidermis revealed slight hyperkeratosis, acanthosis and a moderate degree of follicular plugging. The basal cell layer was intact. Mild spongiosis of the rete ridges in the region of the cysts was seen. The rete ridges gave evi-

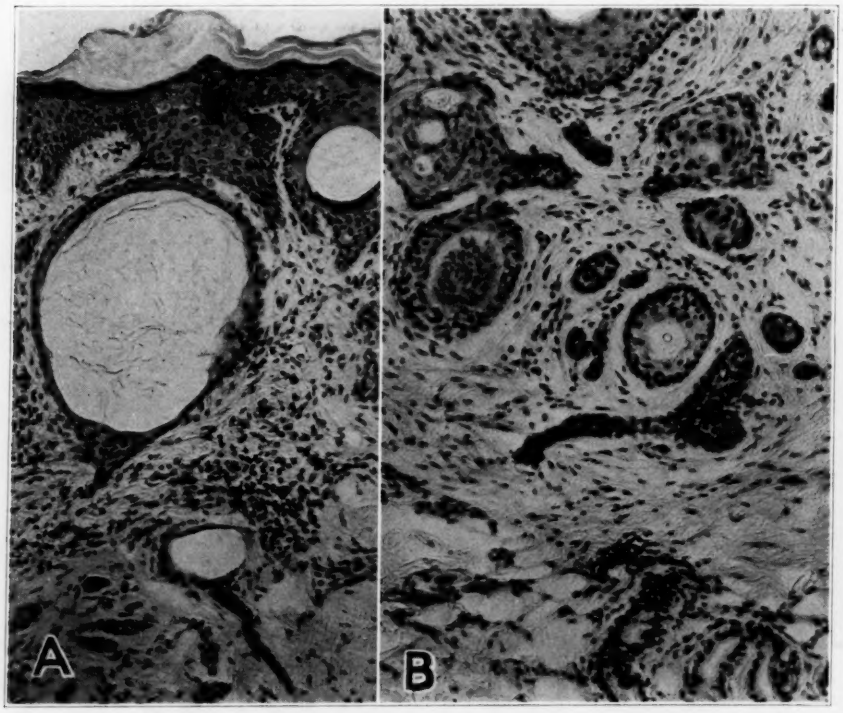


Fig. 2.—*A*, beneath the epidermis, which contains cysts, is the lumen of a sweat duct which has undergone cystic change. Cellular infiltration and homogenization of connective tissue may be noted (hematoxylin and eosin; × 130). *B*, budding and proliferation of the hair follicles; a sweat duct may be seen with beginning cyst formation and a narrow strand of epithelial cells. Relatively normal sweat glands can be seen in the lower right corner (hematoxylin and eosin, × 140).

dence of marked proliferation in depth and width; some extended in bands deep into the cutis, and many presented bulblike swellings with degeneration of the central portion and formation of cysts. An occasional mitotic figure was seen. Some of the rete ridges were continued into long processes, resembling proliferated, hypertrophied sweat ducts with a basal layer arrangement of the peripheral layer. Islands of atypical sebaceous cells were found irregularly in the epidermis,

hair follicles and walls of the cysts and occasionally also in hyperplastic tissue resembling sweat ducts. The hair follicles gave evidence of hyperplasia, budding and the formation of central cysts. Not all of the follicles contained hair; they possibly were simply artefacts.

The cysts ranged in size from microscopically to macroscopically visible cysts 2 mm. or more in diameter. They varied from small areas in the epithelial strands to large homogeneous cysts, with well defined walls. The content of the cysts was in some instances lamellated or concentric and in others homogeneous. When the cysts were situated in the epidermis proper, they were walled by the epidermis: when situated in the rete ridges or in the hyperplastic cell strands, the walls

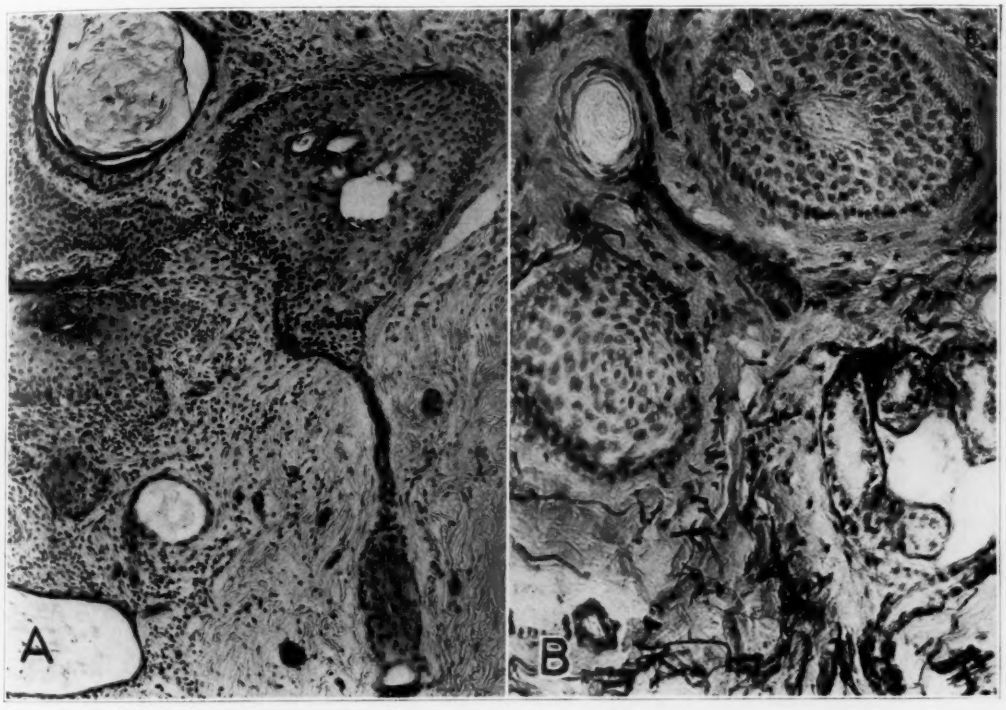


Fig. 3.—*A*, a formation resembling a sweat duct, with a longitudinal lumen joining a hair follicle. Large, thin-walled cysts and lymphocytic infiltration also may be seen (hematoxylin and eosin; × 200). *B*, a cyst (upper left corner) united with a sweat duct and possibly connected to the sweat gland in the lower right corner. A definite membrana propria may be seen about the sweat gland. In the upper right corner is a hair follicle with beginning cyst formation (elastin H; × 200).

consisted of several layers of epithelial cells with an outer basal cell layer. Toward the center there was no sharp margin. The cysts situated deeper in the corium had only two or three layers of flattened cells resembling sweat duct cells. These cysts had no membrana propria. A fairly large number of cysts in the cutis disclosed the formation of buds with sweat ducts, the starting point for the formation of epithelial strands. Throughout the cutis there was an abundance of epi-

thelial strands, irregularly arranged and extending in all directions. Many of the strands had definite lumens. In single sections many of the cell strands seemed to be isolated, but in serial sections they revealed connection with the epidermis on the one hand or with the sweat ducts or cysts on the other, or occasionally with hair follicles. The connection of these strands of cells with the sweat glands could not definitely be demonstrated. The latter had slightly dilated lumens, and in most sections their number was small in proportion to the number of sweat ducts. In some of the sections they were even absent. There was an infiltrate composed chiefly of lymphocytes, with some plasma cells, in the upper part of the cutis in the vicinity of the cysts, hair follicles, strands of cells and perivascular regions. The connective tissue was increased in amount, and stains for mucin revealed moderate deposits of mucin throughout the upper and middle parts of the cutis and especially around the cystic areas and in the cysts. There was a homogeneous appearance of the connective tissue in limited areas. The elastic tissue revealed a decrease in number and a thinning of fibers where the cysts and epithelial strands were present but was well preserved otherwise. The vessels gave evidence of dilatation where infiltration occurred and of deposits of hemosiderin in their vicinity. Occasional obliteration of their lumens was seen. A foreign body giant cell reaction was seen about a few of the cysts, possibly about degenerating sebaceous glands.

The specimens for biopsy removed from the back of the finger presented no essentially different appearance from those taken from the back, but the changes were less marked. The formation of epithelial processes from the epidermis was less frequent. There were marked proliferation and budding of the hair follicles, with formation of cysts, and associated hyperplastic epithelial processes from sebaceous glands, also with formation of cysts. Besides the ordinary sebaceous glands there were a few hypertrophied glands. The sweat glands were numerous, as is the case normally in the finger. The gradual increase in the thickness of the sweat ducts, as they approached the epidermis, was observed. In transverse section they could repeatedly be seen to consist of many layers of cells concentrically arranged around a lumen. Sections for biopsy from the back and the finger taken three weeks after treatment in the hospital did not give evidence of diminution in the pathologic changes, in spite of the clinical improvement.

Drs. O. H. and H. A. Foerster permitted me to study the specimens for biopsy obtained by them eight months prior to the patient's first admission to the clinic. Sections were taken from the back, thorax, hand and thigh. The sections from the back did not differ essentially from my sections from the same region (fig. 4). The specimen from the thorax revealed only a few hyperplastic rete ridges and cell strands. The hair follicles, with or without hairs, were hyperplastic and budding and showed early formation of cysts. The presence of normal sweat ducts coming into the epidermis was noted. The specimen taken from the hand revealed well preserved rete ridges with degenerative changes of epidermal cell nests and cell strands suggestive of beginning cyst formation. The specimen from the thigh showed one deep hair follicle that contained a cyst near the hair papilla. There were also mild infiltration around the vessels and fibrosis similar to that seen in scleroderma; a diagnosis of scleroderma was considered in the earlier stages of the disease.

In an effort to follow the strands and cell islands and to establish the connection of the cysts and epidermis with the hair follicles and sweat ducts, I undertook to reconstruct the connections in wax from serial sections (fig. 5). The reconstruction method used by Born,[22] with minor variations, was applied. In model *a*,

22. Born, G.: Die Plattenmodelliermethode, Arch. f. mikr. Anat. **22**:584, 1883.

seventy-five serial sections from the same block were used, including those from model *b*, but from a different site in the sections. The rapid change in the pictures made it necessary to use every one of the slides in the two series. A Spencer lantern was used, and the sections were magnified 160 times, the sections being 0.8 micron thick. Drawings were made on paper, and wax plates were then laid on them and cut. This proved to be an accurate method, as the wax was transparent. The wax plates had to be made 1.3 cm. thick. To make them, I tried a roller at first, but I found that for such thin plates the exact temperature of the roller was too difficult to control. I therefore melted the wax mixture and poured it on boiling water. The square of the pans multiplied by 1.3 cm. gave the amount

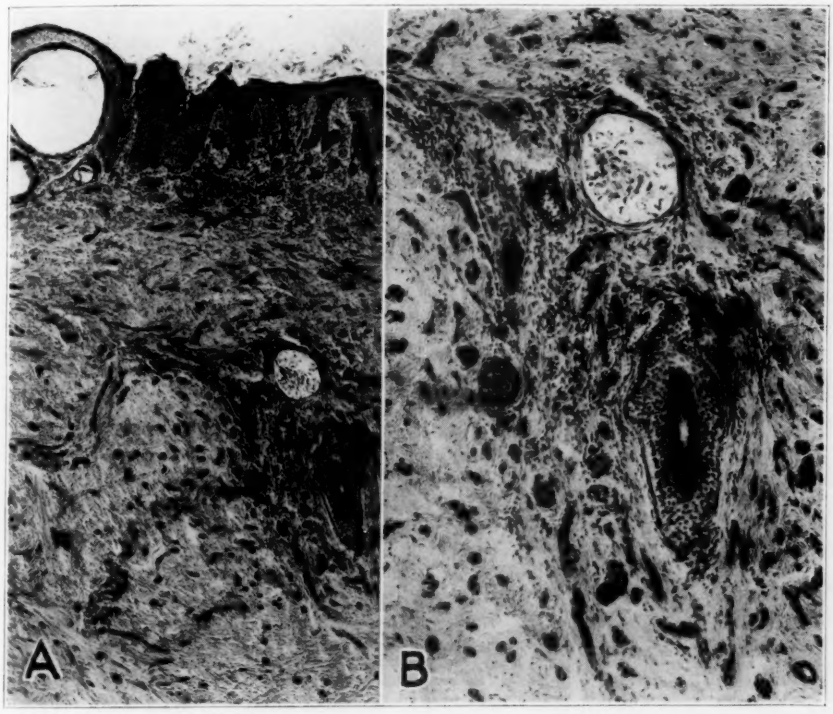


Fig. 4.—The Drs. Foerster permitted me to use this illustration. *A*, a nevoid lesion on the back. There is an epidermal cyst in the upper left corner. Numerous strands resembling sweat ducts and a hair follicle may be seen at the lower right corner (hematoxylin and eosin; × 40). *B*, a large, thin-walled cyst, budding processes from a hair follicle and numerous strands resembling sweat ducts cut transversely and longitudinally (hematoxylin and eosin; × 80).

of wax to be used for each plate. Different mixtures of wax were tried out, but none gave as good results as the following: beeswax 3 parts, paraffin 1 part and resin 0.5 part. This gave a flexible wax plate which was easy to handle. The specific weight of the mixture was calculated, specific weight as given in the "Pharmacopoeia of the United States" being used. The cut plates were placed one on the other and fused together.

The two wax models in figure 5 emphasize the close relationship of the various types of dermatosis under consideration. Model *a* was made to bring out the tricho-epitheliomatous character, and it clearly reveals the extensive epithelial hyperplasia and formation of cysts. It also demonstrates how the cell strands (or hyperplastic sweat ducts) join the hair follicles. The globoid swellings of the hair follicles which enclose cysts can be seen. The model also shows the entrance of a hyperplastic sweat duct into the hair follicle, as shown in figure 3*A*. Model *b* reveals an acanthotic epidermis with prolonged and branched rete ridges and a complex picture of cysts in all stages in the epidermis, in the rete ridges and in the hyperplastic sweat ducts. The last of these could be shown to have a lumen. The bulblike cysts, as described under microscopic observations, were in the following situations: in the (1) epidermis, often with an opening on the surface, (2) rete ridges, (3) prolonged rete ridges, which were passing over into cell strands or sweat ducts in the corium, (4) sweat ducts and (5) branched, hyperplastic hair follicles.

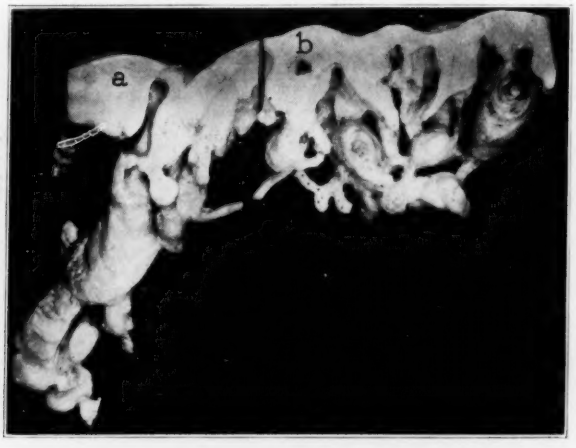


Fig. 5.—Wax models: *a*, budding processes from a hair follicle, some resembling sweat ducts, and *b*, irregular acanthosis and an interrelationship between strands resembling sweat ducts and cysts associated with hair follicles. All of the bulblike formations in *a* and *b* represent cysts.

## COMMENT

The hereditary, familial and even mental factors which are so often found in epithelioma adenoides cysticum but which are absent in syringoma were not present in this case. The distribution and character of the lesions were consistent with epithelioma adenoides cysticum or syringoma. In the cases in which the lesions were confluent, the skin was thickened and almost scleroderma-like. The small and relatively uniform size of the lesions, except the nevoid plaque on the back, was more suggestive of syringoma. In contrast to some patients who have syringoma, the patient's ability to sweat was unchanged. Histopathologic study of the various specimens for biopsy, with wax-models

reconstructed from serial sections, revealed features of both epithelioma adenoides cysticum, including tricho-epithelioma, and syringoma. Consistent with epithelioma adenoides cysticum were the prolongation of the rete ridges, often into narrow strands of epithelial cells, the benign nature of the epithelial hyperplasia, the acanthosis of the epidermis, the presence of cysts in the epidermis, rete ridges, hair follicles and epithelial-lined cysts in the cutis and the origin of the narrow strands of epithelial cells, with or without lumens, from the epidermis and rete ridges and from the hair follicles. The presence of sebaceous cells in the epithelial cell strands is also consistent with epithelioma adenoides cysticum. That syringoma also may indicate involvement of the epidermis has already been mentioned. The pathologic picture of the syringoma in this case is well illustrated in figures 2 *A* and *B* and 3 *B*. Sweat duct strands with lumens and comma-like tails are seen, and in serial sections appear to originate from sweat-ducts. No definite connection with the sweat glands could be demonstrated. Solid, narrow strands of epithelial cells, without lumens, also were seen, corresponding to those depicted by Brooke and Hartzell. The changes in the deposits of mucin and in the connective and elastic tissue, the inflammatory reaction, including the deposits of hemosiderin, and the occasional foreign body giant cell reactions, were consistent with either diagnosis. Hyaline changes in the connective tissue or epithelial cells were not evident, so that cylindroma could be ruled out.

SUMMARY

A case presenting the clinical and histopathologic picture of both epithelioma adenoides cysticum and syringoma is reported. Two wax models reconstructed from serial sections confirmed the diagnosis. Epithelioma adenoides cysticum, tricho-epithelioma and adenoma sebaceum should be regarded as variants of the same condition. The differential diagnosis is given in this case to distinguish the condition from syringoma, cylindroma and nevus sebaceous or senile sebaceous adenoma.

# ELEPHANTIASIS OF THE PENIS AND SCROTUM

## A SEQUELA OF LYMPHOGRANULOMA INGUINALE

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AND
BERNARD PLOCH, M.D.
ST. LOUIS

Lymphogranuloma inguinale, which was first described by Nicolas, Favre and Durand [1] in 1913, has received sufficient recognition in the literature, so that the diagnosis of an acute case in the male should be a matter of little difficulty.

Though late complications are commonly identified in the female in the form of anorectal syphiloma, esthiomene (chronic ulcers of the vulva with elephantiasis) and, in some cases, high rectal stricture, they have rarely been observed in the male. Barthels and Biberstein [2] reported one case of elephantiasis of the penis and scrotum in which the Frei reaction was positive. We were unable to find a similar case recorded in the American literature. Sulzberger and Wise [3] mentioned the possibility of the development of elephantiasis of the penis and scrotum as a sequela of lymphogranuloma inguinale due to localization of the process and retractile scarring.

### REPORT OF A CASE

*History.*—P. G., a white man aged 52, married and unemployed, was a patient in the dermatologic clinic of the St. Louis City Hospital in 1933. His father died at the age of 56 following an operation, and his mother died at the age of 55 of heart disease.

He did not remember having had any diseases of childhood, nor had he had other illnesses, except gonorrhea at the age of 26. Nineteen years before examination a sore appeared on the penis. This healed within a "few days" and was followed within about three weeks by a "lump" in the left inguinal region. The lymphatic glands slowly increased in size for about two weeks, at which time they became slightly painful. The mass in the inguinal region was incised and drained. Healing occurred readily, and a small scar remained.

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From the Department of Dermatology, the St. Louis University School of Medicine.

1. Nicolas, Favre and Durand: Lymphogranulomatose inguinale subaiguë, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274 (Jan. 31) 1913.

2. Barthels, C., and Biberstein, H.: Elephantiasis penis et scroti und Lymphogranulomatosis inguinalis, Beitr. z. klin. Chir. **152**:325, 1931.

3. Sulzberger, M. B., and Wise, Fred: Lymphopathia Venerea, J. A. M. A. **99**:1407 (Oct. 22) 1932.

Five years before examination, fourteen years after the appearance of the sore on the penis and the swollen glands, the skin of the penis began to swell, and blisters appeared on the glans. These broke and discharged a clear fluid. New blisters appeared from time to time. There were no subjective symptoms except that the foreskin frequently became very swollen, tight and painful. The acute swelling subsided for a time, but the glans penis was never entirely free from vesicles except when they were all ruptured as a result of trauma. Each succeeding attack became a little more severe and of longer duration; the present one lasted five months. The scrotum had become enlarged during the several preceding attacks.

About ten years before examination the patient began receiving injections of arsphenamine and mercury. These injections were repeated from time to time before and after the development of the swelling and vesiculation of the penis, on which they had no effect. He stated that his wife was in good health.

The lesion in the quiescent stage, with vesiculation, scarring and moderate edema of the foreskin.

*Examination.*—The penis and scrotum were swollen to about twice the normal size. The skin was edematous and thickened. This condition extended to the base of the penis and onto the pubes. There was a depressed scar in the left inguinal region. No glands were palpable in either inguinal area. The glans penis, which was badly scarred and deformed, was the site of multiple deep vesicles containing yellowish-white and blood-stained lymph. The foreskin, which was greatly thickened, extended over the glans and was retracted with great difficulty. Proctoscopic examination of the rectum revealed no pathologic condition. The prostate was not abnormal.

*Laboratory Findings.*—There were 4,640,000 erythrocytes and 8,300 leukocytes, of which 51 per cent were segmented forms, 45 per cent lymphocytes, 1 per cent stab cells and 3 per cent monocytes; the hemoglobin was 85 per cent. The Kahn reaction was positive.

The Frei test was carried out, active sterile Frei antigen having been obtained from Tomlinson and Cameron. The intradermal injection of 0.1 cc. of the antigen produced an area of erythema and infiltration, which persisted for more than a week. Control tests on normal persons gave negative results.

## COMMENT

Sequelae of lymphogranuloma inguinale, which are frequently encountered in women, are explained on the basis of the site of the primary infection, which is usually the cervix or areas in the vicinity, and of the lymphatic drainage. Rectal stricture, which is occasionally found in the male, is considered to be an extension from the inguinal glands. In view of these not uncommon developments in the other sex, it is strange that there have been no more reports of elephantiasis of the penis and scrotum from this cause. The explanation of this discrepancy may be the fact that in the male usually only one inguinal region is affected, and the collateral lymphatic circulation is ample. On the other hand, in view of the frequency of the acute stage of the disease, it is probable that the condition is not recognized.

Elephantiasis of the penis and scrotum is more likely to occur in cases in which the collateral circulation has been disturbed or in which the entire regional lymph system becomes involved in the pathologic process.

In the histologic study of their case Barthels and Biberstein [2] were able to identify a pathologic structure in the skin of the scrotum which was similar to the histologic picture seen in recent lymphogranuloma inguinale buboes and the same as that seen on the walls of the rectum and the site of the primary lesion. They concluded that the virus of lymphogranuloma inguinale can exert an irritative growth-stimulating influence and that this inflammatory process involves the lymph glands and lymph vessels and extends into the periphery. They also expressed the opinion that the lymph vessels may and on occasions do become thrombosed, with sclerosis finally resulting.

As a result of their investigations they concluded that treatment should be expectant, as removal of the glands may cause harm by destroying the few collateral lymph vessels.

Our case presented features which could most likely be explained on the basis of this type of pathologic process. Though permission for a biopsy was denied, we were able to observe this case clinically over several months. During this time there were several periods of acute swelling and vesiculation of the penis and scrotum. These exacerbations occurred and receded without complete return of the penis or scrotum to normal size and shape. During the periods of engorgement new, deep-seated lymph vesicles appeared on the glans. The process, which had become progressively worse since the onset, seemed to indi-

cate that the condition was spreading gradually to involve a greater and greater area and hence was slowly blocking off the collateral lymph circulation.

SUMMARY

A case of elephantiasis of the penis and scrotum is reported in which the history and positive Frei reaction prove that the primary cause was an infection with the unknown virus of lymphogranuloma inguinale.

The clinical picture is compared to that of chronic ulcers of the vulva with elephantiasis in the female.

Attention is directed to the fact that cases of this type may go undiagnosed.

1143 Missouri Building.

# PUSTULAR PSORIASIS OF THE PALMS AND SOLES

## REPORT OF FOUR CASES

DAVID BLOOM, M.D.
NEW YORK

There is a type of erythematosquamous pustular eruption on the palms and soles which is frequently considered to be due to mycotic infection and is treated as such in spite of negative results of laboratory observations. I feel convinced that this is an atypical form of psoriasis. Its apparent rarity is due to the fact that it is often overlooked as a special entity.

The existence of exudative forms of psoriasis was observed long ago. So-called rupioid psoriasis, the main feature of which is marked exudation, was described as long ago as 1865 by Anderson.[1] In 1877 Kaposi[2] remarked that it was sometimes difficult to differentiate psoriasis from eczema, and he mentioned[3] cases in which eczematous lesions developed on psoriatic plaques. Neumann[4] reported three cases of eczema the lesions of which changed to typical psoriatic patches. Mathieu[5] saw four patients with psoriasis whose condition changed within twenty-four hours to generalized eczema. Nenzioni[6] observed the formation of bullae in a case of acute psoriasis.

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Read at the Annual Meeting of the New York State Medical Society, Section of Dermatology and Syphilology, Utica, N. Y., May 16, 1934.

From the Department of Dermatology and Syphilology of Bellevue Hospital and New York University Medical College, service of Dr. Howard Fox.

1. Anderson, T. M'Call: The Psoriasis and Lepra, London, John Churchill & Sons, 1865.

2. Kaposi, M.: Pathologie und Therapie einzelner Hautkrankheiten, Wien. med. Wchnschr. **27**:1056 (Nov. 3) 1877.

3. Kaposi, Moriz: Pathologie und Therapie der Hautkrankheiten, Leipzig, Urban & Schwarzenberg, 1887, p. 434.

4. Neumann: Beitrag zur Aetiologie der Psoriasis, Allg. wien. med. Ztg. **22**:1 (Jan. 2) 1877.

5. Mathieu, P.: Psoriasis atypique, Thèse de Paris, 1891, cited by Rosenthal, O.: Ueber typische und atypische Psoriasis, Arch. f. Dermat. u. Syph. **25**:79, 1893.

6. Nenzioni, quoted by Riecke, E.: Lehrbuch der Haut- und Geschlechtskrankheiten, ed. 5, Jena, Gustav Fischer, 1920, p. 145.

Cases of generalized pustular psoriasis have been reported by von Zumbusch,[7] Volk,[8] Becker,[9] Hein,[10] Schaefer[11] and Barber[12] and recently in this country by Ebert.[13]

The problem of pustular psoriasis which is localized on the palms and soles has recently received much attention in England, particularly by Barber. Cases of this kind with or without ordinary psoriasis elsewhere on the body have been reported by Koenigsbeck,[14] Ingram,[15] Barber,[16] Gougerot and Eliasheff,[17] Sibley[18] and Wrong.[19]

My interest in this subject was aroused by a patient (case 1) who in September 1927 first attended the New York University clinic for cutaneous diseases and is still under my care at the Bellevue Hospital dermatologic clinic.

## REPORT OF CASES

CASE 1.—*History.*—Mrs. R. H., aged 69, of Irish descent and American birth presented an eruption on the palms and soles of five years' duration. It started with a painful red patch on the right heel and was succeeded gradually by similar lesions on the plantar surface of the great toe and the little toe of the same foot. It was followed by involvement of the right palm, left heel and left palm. In the lesions the patient noticed tiny pustules which dried up after a few days but which recurred constantly, accompanied by pain and itching. The scaly red plaques never disappeared entirely. In the two years previous to the patient's first visit to the clinic the nail of the right great toe started to fall off and regrow.

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7. von Zumbusch, L. R.: Psoriasis und pustuloeses Exanthem, Arch. f. Dermat. u. Syph. **99**:335, 1910.

8. Volk, R.: Ueber atypische Psoriasisformen, Wien. klin. Wchnschr. **24**:1207 (Aug. 24) 1911.

9. Becker, E.: Ein Fall von Psoriasis pustulosa, Inaug. Dissert., Berlin, 1918.

10. Hein: Demonstration of a Case of Psoriasis Pustulosa, Dermat. Wchnschr. **71**:554 (Aug. 7) 1920.

11. Schaefer, R.: Ueber Psoriasis pustulosa (v. Zumbusch), Dermat. Ztschr. **33**:49 (May) 1921.

12. Barber, H. W.: Acrodermatitis Continua vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa, Brit. J. Dermat. **42**:500 (Nov.) 1930.

13. Ebert, Michael H.: A Psoriasiform Eruption with Pustular Exacerbations, Arch. Dermat. & Syph. **27**:933 (June) 1933.

14. Koenigsbeck, Max: Ueber stark exsudative Psoriasis mit Pustelbildung, speziell der Hände, Füsse und Nägel, Inaug. Dissert., Munich, 1917.

15. Ingram, John T.: Acrodermatitis Perstans and Its Relation to Psoriasis, Brit. J. Dermat. **42**:489 (Nov.) 1930.

16. Barber, H. W.: Presentation of Cases of Pustular Psoriasis and Discussion of Same, Brit. J. Dermat. **45**:113 (March) 1933.

17. Gougerot, H., and Eliasheff, Olga: Forme nouvelle de psoriasis: Forme de transition ou mieux associant le "psoriasis microcircinata de Jadassohn" et le "Psoriasis pustulosa:" Forme localizée et fixée, Arch. dermat.-syphiligr. **5**:193 (June) 1933.

18. Sibley, W. Knowsley: Presentation of a Case of "Pustular Psoriasis," Brit. J. Dermat. **45**:322 (July) 1933.

19. Wrong, Norman M.: Pustular Psoriasis, Arch. Dermat. & Syph. **28**:682 (Nov.) 1933.

The patient seemed to be in good health but was overweight. Her past history was essentially unimportant, particularly with regard to cutaneous eruptions. She had two living healthy children. Two children died in infancy of unknown cause and one at the age of 5½ years of diphtheria. Menstruation ceased at the age of 47.

According to the family history one sister suffered from arthritis. Another, who died at the age of 52, weighed 300 pounds (136.1 Kg.) and also suffered from arthritis. One brother, who died of pneumonia at the age of 25, was also obese. The parents died of old age.

No part of the skin was involved except the hands and feet. The center of the right palm, extending somewhat to the thenar eminence, the hypothenar eminence of the left palm and the posterior part of the plantar surface of both heels showed fairly well defined patches, deep red and covered with dry scales and thin crusts. In each patch a few superficial flat yellow pustules ranging in size from that of a pinhead to that of a lentil were seen. From the right heel the

Fig. 1 (case 1).—Exfoliation and remnants of previous pustules after a duration of thirteen years.

eruption extended over the achilles tendon. The inner side of the right great toe and the outer side of the little toe showed similar involvement. The nail of the right great toe was missing, and the same flat superficial pustules were seen in the uneven nail bed. The left foot did not show involvement of the toes or nails.

During her fairly regular attendance at the clinic from September 1927 to May 1932 the most striking feature was the appearance and disappearance of the tiny pustules, which dried up to form tiny scales and crusts of the same size and shape or left a tiny scaly collaret surrounding a superficial opening. The patient complained of pain and marked itching of the palms and soles, particularly with the appearance of a new crop of superficial pustules. Following the appearance of new pustules there were frequently noted, beside the previously described tiny scales, larger flakes, some of which could be partly elevated. Being attached firmly to the skin at one edge they could not be removed, for they seemed to merge gradually with living epidermis. Sometimes exfoliation of a large sheet of epidermis took place, showing thin, red new epidermis beneath (fig. 1).

Repeated mycologic examinations, both microscopically and culturally, gave negative results. The trichophytin test was negative. The pus from the minute pustules was sterile, although repeatedly cultured on different mediums.

The eruption was resistant to any kind of external application. Whitfield's ointment, chrysarobin and tar proved of no value. In fact, the lesions frequently became much worse after such applications. At times acute exacerbations responded favorably to wet dressings of boric acid solution. Roentgen therapy was of no benefit. A paste of crude coal tar in combination with ultraviolet radiation (Goeckerman's [20] method) improved the condition temporarily.

On May 1, 1929, the patient presented on the left elbow a round lesion the size of a quarter which was slightly raised, erythematous and covered with silvery scales. It had the appearance of a psoriatic plaque. This lesion cleared up within a short time under treatment with antipsoriatic ointment.

*General and Laboratory Examinations.*—The patient had enlargement of the heart and sclerosis of the aortic arch. Her blood pressure was 154 systolic and 80 diastolic. The urine was normal except for a faint trace of albumin. The Wassermann reaction of the blood was negative, and the blood count was normal. Chemical analysis of the blood showed: sugar, 100 mg. per hundred cubic centimeters; nonprotein nitrogen, 33 mg., and uric acid, 318 mg. Additional examination of the blood was carried out in the laboratory of Dr. Isadore Rosen, and the results obtained were as follows: calcium, 10.5 mg. per hundred cubic centimeters of serum; albumin, 3.66 Gm. (normal, 4.8 ± 0.3); globulin, 3.09 Gm. (normal, 2.6 ± 0.1); total lipids, 1,460 mg. (normal, 1,510 ± 91); lecithin, 175 mg. (normal, 221 ± 18); total cholesterol, 174 mg. (normal, 212 ± 18); cholesterol esters, 117 mg. (normal, 152 ± 19), and free cholesterol, 32.7 mg. (normal, 28 ± 4).

*Histopathologic Examination.*—The detailed histologic report given by Dr. T. J. Riordan of the lesion on the palm may be summarized as follows: There were parakeratosis, acanthosis, absence of the granular layer, Munro abscesses, intercellular and intracellular edema of the rete, a slight diminution of the suprapapillary layer, wandering cells in the rete and clubbing and fusion of the pegs. These changes, together with the banal inflammatory reaction and the dilated blood vessels in the corium, pointed strongly to a diagnosis of psoriasis. The crusts and a group of closely aggregated micro-abscesses justified the clinical diagnosis of pustular psoriasis (fig. 2).

The skin of the affected heel, which was removed at a stage when no pustules were visible, showed similar microscopic changes typical of the histologic structure of psoriasis except that Munro abscesses were absent.

The significance of the pustules in such cases is particularly well demonstrated in the histologic examination in case 2.

CASE 2.—*History.*—Mrs. M. E., aged 51, of Norwegian descent, came to the clinic of the Bellevue Hospital in April 1934, with a palmar and plantar eruption of nine months' duration. It started on the left palm with a spot on the thenar and another on the hypothenar eminence. About the same time she noticed involvement of the right palm, and a few weeks later both soles were involved. According to the history pustules appeared on reddened skin from the beginning of the illness. They would increase in number and would rupture, disappear and reappear. Following the rupture of the pustules the skin of the affected regions became raw

20. Goeckerman, W. H.: Treatment of Psoriasis, Arch. Dermat. & Syph. **24**:446 (Sept.) 1931.

and dry, cracked along the major lines and caused much pain. The plaques themselves had never cleared up. At times there was intense itching of the palms and soles.

Examination revealed involvement of both palms, the palmar surface of the thumb and wrist and the web between the thumb and index finger by an eruption

Fig. 2 (case 1).—A high power photomicrograph illustrating the conglomeration of Munro abscesses.

similar to that described in case 1. There were also tiny superficial openings, apparently remnants of previous pustules. The skin on the dorsum of the distal phalanx of the fourth finger of the right hand was also erythematous and scaly. The nails showed pitting and transverse ridging and had an uneven surface.

The plantar surfaces of the feet were similarly involved (fig. 3). The eruption extended to the toes, the webs and the mesial and external aspect of the sole on each foot and on the left foot to the mesial, external and posterior aspect of the heel. There were tiny openings which looked like remnants of previous vesicles. Several tiny flat superficial pustules were noted, but there were a few which were slightly raised above the level of the skin. The toe-nails were deformed and showed subungual keratosis.

The patient had suffered from diabetes for the last five years, for which she had received insulin. On the last examination the blood was found to contain 360 mg. of dextrose per hundred cubic centimeters.

Fig. 3 (case 2).—Marked eruption involving the plantar surface of the toes.

The patient had three living healthy children. Four children died at birth owing to instrumental delivery. Her mother was 86 years old and well; her father died at the age of 30 of pneumonia. There was no chronic illness or cutaneous involvement in the family.

*General and Laboratory Examinations.*—No other skin lesions were found elsewhere on the body. General physical examination did not reveal any manifest abnormality except a moderately hyperplastic thyroid gland and a somewhat low blood pressure, the systolic being 115 and the diastolic 70.

The Wassermann reaction of the blood was negative. The blood count was as follows: erythrocytes, 4,350,000, and leukocytes, 5,600, with polymorphonuclears,

48 per cent, metamyelocytes, 5 per cent, transitional cells, 2 per cent, and lymphocytes, 45 per cent. The hemoglobin was 70 per cent.

No fungi were found in the scrapings from the soles and the toe webs and no bacteria was found in the pus. The trichophytin test was negative.

*Histologic Examination.*—The histologic examination made by Dr. T. J. Riordan of the affected skin of the heels revealed the following changes: The rete was greatly thickened both in depth and in breadth. Many of the pegs were fused, but clubbing was not distinctive. A thick scale surmounted the rete, and at one end there was a crust. The corium was edematous and showed sparse general infiltration in the papillary layer. In addition, there were some small foci of perivascular infiltration.

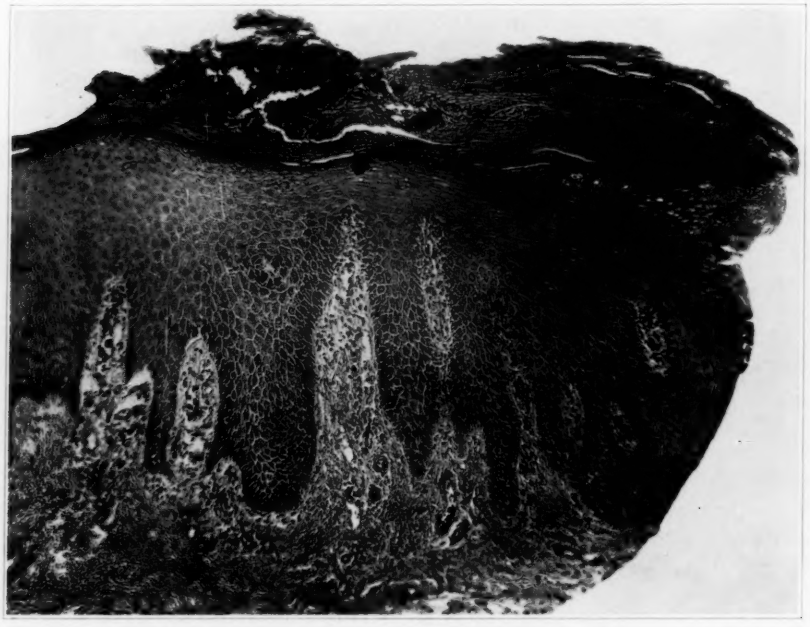

Fig. 4 (case 2).—A low power photomicrograph showing the histologic change in skin from the heel. Note particularly the crust on the left end and the wedge-like conglomeration of Munro abscesses on the right end of the corneous layer.

Under the high power lens there was diminution or absence of the granular layer. Where this layer was absent the corneous layer was uniformly parakeratotic. At one end of the section at the junction of the rete and the corneous layer were numerous small spaces filled with cells. This conglomeration of spaces diminished as the inner portion of the section was approached (fig. 4). The cellular elements within the spaces appeared like small round cells. At the inner side small balls of keratin separated the spaces, and the conglomeration was also separated from the overlying parakeratotic scale by balls of keratin. Above and to the inner side of this conglomeration was a crust of dark-stained cells and débris, floored by a parakeratotic scale and topped by a scale which was ruptured. Intercellular edema, acanthosis, high papillary inclusions and wandering cells com-

pleted the features of the rete. The corium showed no additional noteworthy changes. The cells forming the infiltration were mainly round cells.

*Comment.*—The small spaces were Munro abscesses. The conglomeration of these micro-abscesses at one end with the presence of the overlying adjacent crust could be interpreted as the formation of the pustule. The observations favored confirmation of the clinical diagnosis pustular psoriasis.

CASE 3.—M. B., an American girl aged 11, came to the dermatologic clinic of Bellevue Hospital on March 27, 1934, with an eruption on the hands and feet of two months' duration. No exact information could be obtained about the beginning of the condition.

There was involvement of the palmar surface of the left thumb extending somewhat beyond the metacarpophalangeal crease involving also the web of the thumb and index finger and extending somewhat on the dorsal aspect. The eruption consisted of a fairly well defined, erythematous, fissured, dry, scaly patch. No pustules were seen. . On the palmar aspect of the metacarpophalangeal joint of

Fig. 5 (case 3).—Pitting of all the finger-nails and erythematoscaly eruption on the dorsal aspect of the distal phalanx of each finger.

the third finger of the same hand were a pronounced crease, erythema and slight scaling of the skin. The dorsal aspect of the last phalanges of almost all the fingers of both hands was similarly affected. All the nails were pitted (fig. 5).

The eruption of the feet looked very similar to that described in the two previous cases. Almost the whole distal part of the right sole was affected, involving the plantar surface of the toes and the webs and extending to the instep. The heel was not involved on the plantar surface, but the skin over the achilles tendon was involved. The webs between the fourth and fifth and the third and fourth toes were macerated. The left foot was similarly involved except that only a part of the distal portion of the sole was involved. Also, the lesion extended to the plantar surface of the toes, and the webs were fissured and macerated. Over the instep was an erythematous, somewhat raised plaque the size of a 5 cent piece which was slightly irregular in outline.

All the toe-nails were shortened, yellowish, discolored, brittle and irregularly thickened and showed subungual keratosis. The nail of the great toe of the left foot was missing. It fell off three weeks previous to examination. The proximal part of the nail bed was covered with a soft, uneven horny mass.

Mycologic examination of scrapings of the soles, nails and webs of the toes gave negative results repeatedly. Because of the patient's refusal to cooperate no other laboratory examination could be carried out.

Her family and personal history were negative. Examination in the pediatric department, particularly with regard to a possible focus of infection, revealed nothing abnormal.

During the last few weeks the appearance and disappearance of the flat pustules described in the other cases was again noted.

Case 4.—Mrs. A. B., aged 51, a private patient, was referred to me by Dr. J. V. Shermak of Stamford, Conn., on May 4, 1934. She had had the eruption on the right heel for the past eighteen months. It gradually extended from the region over the achilles tendon to its present size, involving the plantar surface and both sides of the heel. Here again the history of the characterstic periodic appearance of the tiny pustules was obtained. There was also the history of negative results of tests for fungi and of absolute resistance to ointments and to roentgen treatment.

She gave a history of thyroidectomy one and a half years previous to the appearance of the cutaneous lesion. The family history revealed that her mother died of tuberculosis.

Six days following the first examination, when a photograph of the lesion was to be taken, surprising improvement was noted. The plantar surface of the heel looked almost normal, and no pustules were seen anywhere in the involved area. A photograph could therefore be taken only of the side of the heel. This improvement was not surprising to the patient, for such a change took place frequently with or without any previous application of boric acid ointment.

## DIFFERENTIAL DIAGNOSIS

The features of the reported cases correspond to the description of palmar and plantar pustular psoriasis given by the aforementioned authors. These features distinguish this condition from other dermatoses frequently found in these locations. Particularly the strange periodicity in the recurrence of the characteristic primary pustules, the extreme resistance to any treatment and perhaps the frequent involvement and loss of nails suffice to differentiate this lesion from mycotic and amycotic eczema. In addition, the negative mycologic and trichophytin tests, the absence of spongiosis and the presence of the uniform parakeratosis in the histologic picture together with other histologic features characteristic of psoriasis would surely exclude the diagnosis of eczema.

Pustular psoriasis must also be differentiated from acrodermatitis continua, described first by Hallopeau [21] in 1890. This differentiation was considered by Barber,[12] Ebert and others and recently by Andrews.[22]

21. Hallopeau, M. H.: Sur une asphyxie locale des extremités avec polydactylite suppurative chronique et poussées éphémères de dermatite pustuleuse disséminée et symétrique, Bull. Soc. franç. de dermat. et syph. **1**:39 (June) 1890.

22. Andrews, George C.; Birkman, Frederic W., and Kelly, Richard J.: Recalcitrant Pustular Eruptions of the Palms and Soles, Arch. Dermat. & Syph. **29**:548 (April) 1934.

After having read numerous descriptions of cases of acrodermatitis continua in the literature, I am impressed with the clinical resemblance of the disease to pustular psoriasis. Moreover, the condition is frequently associated with frank psoriasis elsewhere on the body. I agree, therefore, heartily with Strandberg [23] and other authors who have expressed the belief that pustular psoriasis and acrodermatitis continua are identical. One imporant differential point, namely, the presence of staphylococci, which was first the contention of Hallopeau, was later disputed by many who found the primary efflorescence sterile. My view is that in at least a great number of cases reported under that name the condition is pustular psoriasis and that it is only the degree of exudation which marks the eruption in some of those cases as being different clinically from pustular psoriasis. Darier [24] divided the cases described under the name of Hallopeau's disease into two different groups. One consisted of cases of so-called benign vegetating pemphigus. The second group of cases, of the condition which Audry named "phlycténose récidivante," comprised, according to Darier, instances of a number of different distinct conditions. Ingram [15] also divided those cases into two groups. One was the infective group, consisting of cases of chronic pyogenic dermatitis. The second, the noninfective group, Ingram considered as comprising cases of pustular psoriasis. Some of these cases reported by him are almost identical with those reported in this paper.

Last but not least, the cases described by Andrews [22] must be dealt with. Clinically they differ from my cases by the presence of vesicles and by the fact that in most of them there was a focus of infection, the removal of which cured or improved the condition in some. Histologically there is a marked difference in many points: 1. The parakeratosis which was very slight in some sections in Andrews' cases was uniform in my cases. 2. The granular layer was prominent and wide in his cases and absent or diminished in mine. 3. The intra-epithelial pustules described and photographed by Andrews were real pustules while in my cases the pustules could be demonstrated as subcorneal conglomerations of Munro abscesses. 4. In one case of Andrews', intra-epithelial vesicles were seen, while no formation of vesicles was seen in my sections. Disregarding these differences, the cases resemble each other both in clinical appearance and in mycologic and bacteriologic observations. I believe, therefore, that at least a number of Andrews' cases are examples of pustular psoriasis. To my mind it is not absolutely impossible that even in those cases in which the formation of vesicles was noted clinically the condition might belong to the group of pustular

23. Strandberg, James: Acrodermatitis continua, Acta dermat.-venereol. **6**:314 (Oct.) 1925.

24. Darier, J.: Acrodermatitis Continua Hallopeau, Proc. Internat. Cong. Dermat., 1930, p. 1198.

psoriasis.[25] Haslund[26] remarked that sometimes the outpouring of serous exudate in conjunction with a more marked degeneration of epithelial cells may so exceed the other features that one must speak of a "vesicle filled with pus." I agree with MacKee, who in the discussion of Andrews' paper remarked that "judging from the description of his clinical material and especially judging from the photographs thrown on the screen I believe that many, if not most, of his cases represent psoriasis pustulosa."

### COMMENT

Pustular psoriasis differs from ordinary psoriasis only in the degree of cellular exudation. When the Munro abscess is increased in size or when a number of Munro abscesses conglomerate the so-called micro-abscess becomes a macro-abscess, manifesting itself clinically as a pustule. The striking feature of the persistent periodic appearance of these pustules and their drying, to form thin crusts, may also be explained from the point of view that one is dealing with psoriasis. Haslund, who defined psoriasis as a process of "suppuration" and who considered this cellular exudation and the formation of "abscesses" as the most characteristic change of the epithelium in psoriasis, called attention to the periodicity of this process. The wandering of leukocytes and the formation of "abscesses" is, according to him, an intermittent process, repeating itself constantly after shorter or longer intervals.

Because of unknown factors the so-called "suppuration" is increased in cases of pustular psoriasis. The pathogenic factor producing psoriasis may be conceived as particularly active in these cases. It seems to me, therefore, that the endeavor to solve the obscure problem of psoriasis should be particularly directed to the cases in which there is exudation, to which group pustular psoriasis belongs.

### SUMMARY

Four cases of an erythematosquamous pustular eruption of the palms and soles are reported. They were strikingly alike in the clinical picture, the course and the result of laboratory examinations.

The most striking clinical feature was the persistent recurrence of tiny, flat, superficial pustules.

The duration of the eruption was very long, varying from four months to thirteen years. During this time the plaques never disappeared.

The eruption was extremely resistant to treatment with ointments and roentgen rays.

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25. In several additional cases observed since this paper was prepared some minute vesicles were present.

26. Haslund, Paul: Die Histologie und Pathologie der Psoriasis, Arch. f. Dermat. u. Syph. **114**:427, 1912.

Mycologic and bacteriologic examinations gave negative results and trichophytin tests which were carried out in two patients were negative.

One patient had diabetes and another had undergone a thyroidectomy a year and a half before the appearance of the eruption.

Histologic examination in two cases confirmed the diagnosis of psoriasis and brought out clearly the significance of the pustule.

Pustular psoriasis differs from ordinary psoriasis only in the degree of exudation.

135 East Fiftieth Street.

# LONG INCUBATION PERIOD OF WARTS

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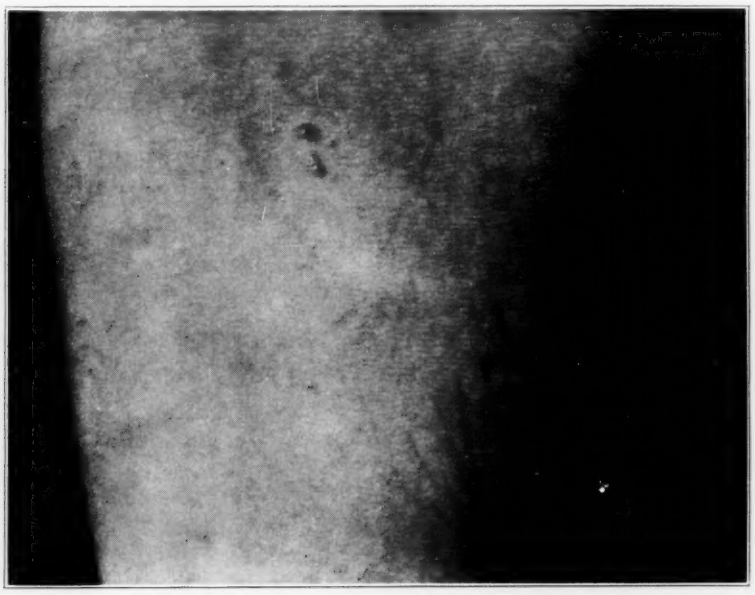
OAKLAND, CALIF.

While doing some work with the lysate therapy of warts, we discovered two cases in which there was a prolonged period of incubation between the experimental inoculation of the wart lysate and the development of the wart.



Photograph of warts which developed one year following an inoculation of wart lysate.

Warts of the common variety had been curetted from many patients and had been sent to Dr. T. D. Beckwith, professor of bacteriology at the University of California. He had prepared a lysate by grinding warts in a physiologic solution of sodium chloride and filtering the mixture through a Berkefeld N filter. We attempted to discover the thermal death point of the wart virus by heating portions to 50, 55, 60 and 65 C. in a water bath for one-half hour. Six human volunteers were given an intradermal injection of each of these heated fractions

From the author's clinic of dermatology at the Cowell Memorial Hospital, University of California.

and also an injection of the unheated Berkefeld filtrate. The sites of inoculation were observed for six months. As no warts had developed at the end of this time, we felt that our experimental inoculations had failed.

The inoculations were performed in September 1932. In September 1933 one of the volunteers showed me two warts which were developing on her arm. The largest, as shown in the accompanying illustration, was at the site of the inoculation of the unheated Berkefeld filtrate. The smaller one was at the site of the inoculation of the Berkefeld filtrate which had been heated to 50 C. A year passed, and none of the fractions heated to higher temperatures had produced warts.

In May 1934, twenty months after the inoculation, a second volunteer had a wart at the site of the inoculation of the unheated fraction. At the time of writing no further warts have developed.

## CONCLUSIONS

Although our experiments have not conclusively demonstrated the thermal death point of the wart virus, we can state that it is probably somewhere above 50 C.

The incubation period of warts experimentally produced may be as long as twelve or twenty months.

# Clinical Notes

## PITYRIASIS ROSEA

### Report of a Case with Lesions of the Palms and Soles

HARRY BAILEY, M.D., HARTFORD, CONN.

Combes [1] and Weber and Rattner [2] have recently called attention to clinical variants of pityriasis rosea with lesions of the palms and soles. In Combes' case the lesions clinically resembled early palmar syphilids, and in Weber and Rattner's case they were similar to vesicular ringworm infection. Another case is herewith reported.

Fig. 1.—Lesions on palms.

Fig. 2.—Lesions on soles.

REPORT OF CASE

A married man, aged 35, was seen on Jan. 5, 1934, with an eruption of ten days' duration. On the trunk, neck and extremities he presented a generalized salmon-colored, scaly macular and papular eruption, typical of pityriasis rosea. Some of the lesions were discrete; others were confluent. On the palms (fig. 1) there were lesions of the maculopapular type, reddish, slightly elevated and infiltrated. Many of the lesions showed a collaret scale. On the soles (fig. 2) there were lesions with the same characteristics, and in addition there was considerable edema about the ankles, insteps and dorsal surfaces of both feet. Clinically, the

1. Combes, F. C.: Pityriasis Rosea: Report of a Case with Lesions of the Palms and Soles, Brit. J. Dermat. **44**:586 (Dec.) 1932.

2. Weber, L. F., and Rattner, Herbert: Clinical Variants of Familiar Diseases of the Skin, Arch. Dermat. & Syph. **28**:190 (Aug.) 1933.

lesions resembled early palmar and plantar syphilids. There was marked itching, especially in the inguinal regions. The Wassermann and Kahn reactions were negative. The patient was treated with hot baths, followed by soothing applications and by the application of 3 per cent salicylic acid ointment. The entire eruption disappeared in about twelve days.

My associate and I were unable to recover the fungi from the lesions on the hands and from the digital interspaces of the feet. Examination of the urine for albumin gave negative results.

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## A SIMPLIFIED METHOD OF PREPARING PENCILS OF CARBON DIOXIDE SNOW

DAVID BLOOM, M.D., NEW YORK

Carbon dioxide snow, which was introduced by Pusey [1] in 1907, has proved a valuable remedy, particularly in the treatment of angiomas, pigmented nevi and lupus erythematosus. Many dermatologists for convenience have discarded the liquid carbonic acid tanks formerly used, employing commercially prepared carbon dioxide snow, from which, by means of a hammer and chisel, pencils of the desired size and shape are prepared.

Recently I found that pencils can be prepared rapidly and conveniently from carbon dioxide snow with a copper tube. I use for this purpose one of the tubes from the cold cautery set of Lortat and Jacob. When the hollow of the warmed tube is pressed against the carbon dioxide snow, a pencil can be made in a few minutes. If the tube becomes cold, it may be removed from the snow and warmed. The size and shape of the tube determine the size and shape of the pencil.

The easy cutting of the snow by the metal tube is due to the great difference between the temperature of the carbon dioxide snow and that of the metal tube, which is a good conductor of heat. Because of its high conductivity for heat, copper, next to silver, is the best metal for this purpose.

135 East 50th Street.

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From the Department of Dermatology and Syphilology, University and Bellevue Hospital Medical College, service of Dr. Howard Fox.

1. Pusey, William Allen: The Use of Carbon Dioxide Snow in the Treatment of Nevi and Other Lesions of the Skin, J. A. M. A. **49**:1354 (Oct. 19) 1907.

# Minor Notes

## VACCINATION FOR HERPES

FREDERICK R. SCHMIDT, M.D., CHICAGO

Recurrent attacks of herpes simplex are a source of great annoyance to many persons. The following simple procedure has brought relief to several patients, and I hope that this report will stimulate physicians to use the method. In this way a fair evaluation of its worth is assured.

Patients seen for the first time during an attack of herpes are given a soothing topical application and told to return to the office at the first sign of the next attack, before the vesicles have broken. The blister fluid is obtained by puncturing the vesicle with a small scalpel and immediately scarifying the skin with this material. The inner side of the thigh is usually selected for the site of vaccination, and after the skin is cleansed with alcohol the blister fluid is scratched into the epidermis by a few gentle strokes of the knife.

I have treated eight patients in this manner, all of whom suffered from facial herpes. Four have not returned for observation, though each patient is told to return to the office at the first sign of a fresh attack. Two patients received a second inoculation and have had no further trouble. The other two have remained free from herpes over a period of two years. The two patients receiving a second vaccination failed to show any reaction after their first treatment. By reaction is meant a zone of redness with some warmth and elevation of the skin. One patient suffered a generalized reaction four hours after vaccination. She said that she felt "sick to her stomach and had a chilly feeling."

The German literature is replete with articles on vaccination for herpes. Percutaneous rubbing is probably as efficacious as scarification, but the type of local reaction is that of a folliculitis.

## UNUSUAL LOCATION OF HERALD PLAQUE OF PITYRIASIS ROSEA

HAROLD SHELLOW, M.D., CHICAGO

The occurrence on the glans penis of the herald plaque of pityriasis rosea is extremely rare. Two such cases are herewith reported.

CASE 1.—A man, aged 32, presented an oval, macular and slightly papular lesion on the dorsum of the glans penis, extending from the edge of the meatus to the corona. The lesion was violaceous, except for the periphery, which was lighter. The central portion was covered by a fragmented, rather firmly adherent, dry scale. There was moderate itching. Two weeks later there was a typical general eruption of pityriasis rosea. The herald patch, although still visible, had faded considerably. The patient had an attack of pityriasis rosea four years prior to this attack, and at that time the herald patch appeared on the back about one week before the general eruption.

CASE 2.—A man, aged 36, presented himself because of an itchy lesion on the glans penis of three days' duration. The lesion, which was sharply outlined and oval, was located between the meatus and the sulcus and extended half-way around the circumference of the glans. It was bright red, being darker in the center, and was rather edematous. The surface was glistening and had a moist appearance. The edge of the lesion was raised distinctly above the surrounding area, to form a ring. Nine days following the appearance of the penile lesion an eruption developed on the patient's body which consisted of pink and fawn-colored scaly lesions varying in size from that of a pea to that of a coin; they assumed the distribution along the lines of cleavage which is characteristic of pityriasis rosea.

185 North Wabash Avenue.

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## PELLAGRA FOLLOWING REACTION FROM THE ROENTGEN RAYS

HERBERT RATTNER, M.D., CHICAGO

I recently saw a woman with pellagra the etiology of which was very unusual. She was 35 years of age and unmarried and had been operated on for carcinoma of an ovary. One month later she was given high voltage roentgen therapy to the pelvis, and after several treatments severe diarrhea, nausea and repeated vomiting of the contents of her stomach developed. This persisted for several weeks to the point where she was almost prostrated. The reaction subsided slowly, and when I saw her after about six weeks of repeated vomiting she had dermatitis of the face and hands, a red beefy tongue and diarrhea, and she was "extremely nervous." The picture was typical of pellagra. She had been exposed to the sun for only a few minutes each day. The cause for the pellagra in this case seemed obvious; there was no avitaminosis in its usual meaning. When, after a time, the patient was able to retain her food (her diet had not been changed) she recovered rather quickly.

7 West Madison Street.

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## AERATED SHOES

LESTER HOLLANDER, M.D., PITTSBURGH

Among the various factors which play a part in the recurrence of infections of the foot due to fungi and streptococci, hyperhidrosis is undoubtedly an important one. The ordinary shoe, which encases the foot, tends to exaggerate the maceration of the epidermis associated with perspiration. The so-called aerated shoes (with the top perforated by many small holes) tend to overcome hyperhidrosis and to keep the feet much drier. A number of my patients wear this type of shoe exclusively during the warmer months, with most beneficial results.

631 Jenkins Building.

# Correspondence

## PRURITUS IN CHRONIC PEMPHIGUS

*To the Editor:*—In view of the recent report in the ARCHIVES (**30**:843 [Dec.] 1934) by Prinzmetal on the use of nitrites for the relief of pruritus, it may be of interest to record the effect of erythrol tetranitrate on a patient with chronic pemphigus. The patient, a Jewish housewife, aged 43, had presented extensive bullous lesions characteristic of pemphigus vulgaris for nineteen months. The lesions had gradually extended until four months ago, when she was admitted to the Royal Victoria Hospital at Montreal. The eruption was generalized. The mucosae and the genitals were free from lesions. The Pels-Macht test was made, the result being 54 per cent. Severe toxemia was present.

A marked feature of the disease was an associated pruritus and burning. This gradually became more severe, until it was almost unbearable. Sleep was possible for her (and for the remainder of the patients in the ward) only when she was given various combinations of morphine, codeine, phenobarbital, bromides and sodium amytal. More or less as a last resort she was given erythrol tetranitrate in the dosage suggested by Prinzmetal. The effect was truly spectacular. Within forty minutes the pruritus and burning had disappeared. In another twenty minutes the patient was asleep. Since that time it has been possible, in a large measure, to control the distressing cutaneous symptoms. Habituation occurred, but temporary discontinuance of the drug again enhanced its effectiveness. Dosages up to 1 grain (0.065 Gm.) were used from one to four times daily.

Interestingly enough, the lesions started to regress soon after the treatment was instituted, and at the present time the patient shows considerable improvement over her previous condition. Whether the nitrates actually caused the regression of the lesions is a moot question, but certainly the remarkable amelioration of symptoms following their use justifies their inclusion in the therapeutic armamentarium for this most serious of cutaneous diseases.

FRANK E. CORMIA, M.D., Montreal, Canada.

# Abstracts from Current Literature

WHAT TREATMENT IN EARLY SYPHILIS ACCOMPLISHES: I. RELAPSE AND CURATIVE RESULTS; II. OPTIMUM TREATMENT; III. COMPARISON OF BRUUSGAARD'S WORK AND THE 3- TO 20-YEAR RESULTS OF THE COÖPERATIVE CLINICAL GROUP. J. H. STOKES, L. J. USILTON, H. N. COLE, J. E. MOORE, P. A. O'LEARY, U. J. WILE, T. PARRAN JR. and J. MCMULLEN, Am. J. M. Sc. **188**:660 (Nov.) 1934.

The authors consider the frequency and type of all forms of relapse in early stages of syphilis. The total incidence was found to be 10.1 per cent for all patients treated for any period of time, the maximum being 19.7 per cent for patients treated six months or longer.

The highest incidence of relapse was found to occur in patients with the mucocutaneous type of the disease who received treatment in the primary stage when the serologic reaction was positive. The explanation offered is that at that stage the immunizing or protective effect of a general secondary reaction is lacking.

It may be to the advantage of this type of patient to allow the condition to progress to secondary syphilis if continuous treatment is available, provided due regard for infectiousness is considered. Otherwise a patient with primary syphilis who shows a positive reaction must be doubly vigilant regarding treatment and relapse.

In this study the terms "satisfactory results" or "cure" indicate a long series of negative tests of the blood, often a negative test of the spinal fluid, no recent clinical or serologic evidence of relapse and normal results of physical examination.

Without regard to the amount or method of treatment satisfactory results were obtained in 52.7 per cent of cases observed for two years or longer.

In cases of primary syphilis with a negative serologic reaction the cures amounted to 86.4 per cent after continuous treatment; the figure, however, dropped to 64.3 per cent if the reaction of the blood had become positive in the primary stage of the disease. In patients with primary syphilis and a negative serologic reaction even irregular treatment gave satisfactory results in 54.7 per cent of instances.

When secondary syphilis had developed the continuous method of treatment carried on for two years and over resulted in satisfactory results in 81.5 per cent of the cases.

A theoretical discussion is given regarding the reasons why certain forms of continuous treatment give better results in certain stages of the infection, according to the function of resistance and the interval between courses of treatment.

In a consideration of the optimum treatment it was found that the greatest percentage of satisfactory results followed a course of from ten to nineteen injections of arsphenamine with the accompanying amount of preparations of heavy metals administered in the primary stage of the disease when the serologic reaction was negative. When the serologic reaction had become positive, from twenty-five to thirty-five injections of arsphenamine were required, and in early cases of secondary syphilis (first year) from twenty to twenty-nine injections were needed. The percentage of satisfactory results was 85, 65 and 58 per cent, respectively, the poorer results obtained in some cases being due to the intrinsic resistance of the disease.

It is believed that a low dosage of arsphenamine is less valuable than the higher dosage, the incidence of neurosyphilitic relapse being higher with low dosage and intermittent treatment, while proper treatment with arsphenamine did not predispose to neurosyphilis. "Low dosage" refers to from 0.2 to 0.45 Gm. for males and from 0.2 to 0.3 Gm. for females.

Regardless of the system used preparations of heavy metal with at least twenty injections of arsphenamine should be used during the first two years of the disease. If satisfactory results are not obtained more arsphenamine should be given.

If during a two year period of treatment the patient has progressed steadily to results which are satisfactory clinically and serologically, cessation of treatment is justified.

A comparison is made of 907 cases in which treatment was administered (cooperative clinical series) with 145 cases of untreated syphilis (Bruusgaard series) observed for from three to ten and ten to twenty years.

In the untreated patients the incidence of neurosyphilis was from two to four times greater, and that of cutaneous and osseous lesions, from seventeen to twenty-six times greater, than in patients who had received treatment.

Likewise, from 77 per cent to 63 per cent of the patients who had received treatment but only from 24 per cent to 36 per cent of those in the untreated series were free from symptoms and showed a negative Wassermann reaction. A small percentage (from 1.2 to 1.5 per cent) of treated patients whose serologic reaction was negative had abnormal reactions of the spinal fluid after from three to twenty years.

In the untreated series 61 per cent were found to be free from symptoms after from three to ten years, while 96 per cent of those who had received adequate treatment were free from symptoms. In the group observed from ten to twenty years the same treatment resulted in freedom from symptoms in 74 per cent of the cases. For untreated patients the figure was 50 per cent.

Irregular treatment was the chief cause of complications.

Bruusgaard found no evidence of cardiovascular syphilis in untreated patients in the group observed from three to ten years, but in the groups observed for longer periods he found that the incidence was 1.5 per cent in the ten to twenty year group and 10 per cent in the twenty to thirty year group.

For the cooperative clinical series of treated patients the incidence of cardiovascular syphilis was as follows: Definite symptoms appeared in 0.7 per cent and suggestive symptoms in 1.3 per cent of the cases in the three to ten year group. In the ten to twenty year group definite symptoms were found in 5.8 per cent and suggestive symptoms in 4.6 per cent.

The members of this clinical group feel that the results obtained fully justify adequate and systematic modern treatment for early syphilis.

THE RELATIONSHIP BETWEEN ANTISYPHILITIC TREATMENT AND TOXIC CIRRHOSIS. C. W. BALDRIDGE, Am. J. M. Sc. **188**:685 (Nov.) 1934.

Twelve cases are analyzed in which no clinical evidence of disease of the liver was found before the institution of antisyphilitic treatment. In ten cases the reaction of the blood was strongly positive, and syphilis had been present for a variable number of years. The number of injections of arsphenamine varied from five to forty-two, and in most of the cases large doses of mercury were administered.

In these twelve patients cirrhosis of the liver with portal obstruction followed the antisyphilitic treatment, the onset of symptoms varying over a period of several years.

DELAYED RESOLUTION IN LOBAR PNEUMONIA AND ITS RELATIONSHIP TO PREEXISTING SYPHILIS. A. WEINSTEIN and M. GOODMAN, Am. J. M. Sc. **188**:716 (Nov.) 1934.

In a series of 509 patients with lobar pneumonia, 37.5 per cent were found to be syphilitic.

The clinical course in these cases was apparently not altered by the presence of syphilis, nor was delayed resolution found more frequently than in nonsyphilitic patients.

Antisyphilitic treatment produced no favorable response in cases of unresolved pneumonia in the presence of syphilis. JAMIESON, Detroit.

THE INFLUENCE OF THE HYPOPHYSEAL HORMONES (PROLAN A AND B) ON CERTAIN DERMATOSES. G. B. COTTINI, Gior. ital. di dermat. e sif. **69**:1653 (Oct.) 1934.

Of forty-four patients observed by Cottini, seven showed prolan in the urine. Of these seven patients, one with generalized alopecia areata showed prolan A; one with Duhring's disease, prolan A and B; one with kraurosis vulvae with spinocellular epithelioma, prolan A; two with leprosy, prolan A; one with vulvar pruritus, prolan A, and one with herpes zoster and cerebrospinal syphilis, prolan A. These results are in accord with those of other investigators who have demonstrated the presence of large amounts of prolan A in the urine of a number of patients with varied dermatoses. The diverse nature of the cases of dermatoses in which prolan is found points to the possibility that the elimination of prolan in the urine depends not on the presence of the cutaneous manifestations but on a certain feature common to all these cases. Bertaccini expressed the belief that this phenomenon is due to increased intracranial pressure, but Cottini states that in the cases he reported the pressure of the spinal fluid was normal.

PARDO-CASTELLO, Havana, Cuba.

SOFT ROENTGEN RAYS (GRENZ RAYS) IN THE TREATMENT OF LUPUS VULGARIS. B. SPIETHOFF, Dermat. Wchnschr. **99**: 873 (July 7) 1934.

The soft roentgen rays are particularly suitable for the treatment of lupus vulgaris. The average dose used is 4,600 roentgens, though much higher amounts are used if necessary. The involved area is divided into fields of not more than 3 cm. in diameter, and the surrounding area is protected by 1 mm. of leaded rubber. Recently a preliminary irradiation with ultraviolet and infra-red rays has been utilized to enhance the reaction. In spite of the large doses of radiation used, the only after-effects observed in eight years have consisted of atrophy, depigmentation and slight telangiectasia. Several photographs are presented showing the effect of long wave radiation in cases of extensive lupus vulgaris.

VALUE OF SUITABILITY TESTS FOR BAKERS IN THE FIELD OF INDUSTRIAL DIRECTION. ERNA ZITZKE, Dermat. Wchnschr. **99**: 878 (July 7) 1934.

Zitzke has demonstrated that the causative factor in bakers' eczema is most often the ammonium persulphate used as a "flour improver." She tested a considerable number (103) of the prospective students of a bakers' school in order to determine whether they were fitted for that occupation. Two gave positive cutaneous reactions, but in neither had eczema developed in the course of one and two years, respectively, though the reaction remained positive. Of the remainder, 14 had a positive reaction, and eczema developed in 8 of these. In 2 eczema developed though the cutaneous reaction remained negative.

SIMULTANEOUS DEVELOPMENT OF LUPUS PERNIO AND LUPUS VULGARIS: THE ETIOLOGY OF LUPUS PERNIO. HANS SÄUFERLIN, Dermat. Wchnschr. **99**:884 (July 7) 1934.

A patient is described who had had lupus vulgaris of the cheek for nine years and typical lupus pernio of the nose for about the same length of time. The patient had had glandular tuberculosis, and there was evidence of pulmonary involvement. The findings indicate a tuberculous etiology for lupus pernio.

VARICELLA AND SENSITIZATION BY LIGHT. A. S. VON MALLINCKRODT-HAUPT, Dermat. Wchnschr. **99**: 917 (July 14) 1934.

Observations by the author tend to show that exposure to sunlight or to artificial ultraviolet radiation increases the number and changes the character of the varicella lesions which develop in the irradiated area.

PUSTULOSIS VACCINIFORMIS ACUTA IN ADULTS. RICHARD FRÜHWALD, Dermat. Wchnschr. **99**:922 (July 14) 1934.

Pustulosis vacciniformis acuta has previously been described as a complication of severe eczema in infants. Frühwald describes three cases, two occurring in patients 18 and one in a patient 20 years old. In all three a rather severe eczema had been present for years. The acute condition started suddenly with a marked rise in temperature and the development of pustules resembling those of variola or vaccinia in the eczematous areas. This acute phase cleared in a few days, leaving the eczema as before. In the three cases the possibilty of an exposure to vaccinia was ruled out.

ATYPICAL DIFFUSE SCLERODERMA WITH OSLER'S SYNDROME AND HEPATIC DYSFUNCTION. WILHELM MILBRADT, Dermat. Wchnschr. **99**:973 (July 28) 1934.

Milbradt observed a woman, aged 47, who suffered from scleroderma associated with sclerodactylia, telangiectasia haemorrhagica hereditaria and a mild cirrhosis. The possibility of an etiologic relationship is discussed.

THE TREATMENT OF LUPUS ERYTHEMATOSUS WITH BISMUTH. A. JORDAN and A. TARABUCHIN, Dermat. Wchnschr. **99**:1145 (Sept. 1) 1934.

Jordan and Tarabuchin report using local applications of a preparation consisting of 20 per cent metallic bismuth, 31.2 per cent quinine and 48.8 per cent iodine in almond oil for lupus erythematosus. It was applied daily, and improvement resulted, though complete cures did not take place.

LOCAL TREATMENT OF CUTANEOUS TUBERCULOSIS WITH OINTMENT CONTAINING OLD TUBERCULIN AND A SALT-FREE DIET. J. DÖRFFEL and W. PASSARGE, Dermat. Wchnschr. **99**:1173 (Sept. 8) 1934.

A concentrated ointment of old tuberculin containing killed bovine and human tubercle bacilli and a keratolytic substance was used with benefit in a number of cases of cutaneous tuberculosis. When the treatment was combined with a salt-free diet the beneficial results were more rapid than when either method was used alone.

A CASE OF ACRODERMATITIS CONTINUA SUPPURATIVA HALLOPEAU. H. SPRAFKE, Dermat. Wchnschr. **99**:1179 (Sept. 8) 1934.

A 30 year old woman presented a typical case of acrodermatitis continua suppurativa Hallopeau which affected the terminal phalanx of the ring finger of the left hand. The condition had been present for over fifteen years and had showed exacerbations. Roentgen therapy resulted in temporary improvement. Eventually amputation of the terminal phalanx was performed, and a cure resulted.

INFLUENCE OF HORMONES ON THE GROWTH OF CUTANEOUS FUNGI (HYPHOMYCETES AND YEAST). H. HRUSZEK, Dermat. Wchnschr. **99**:1184 (Sept. 8) 1934.

Hruszek describes a series of experiments in which he added extracts of thyroid and of anterior lobe of the hypophysis and epinephrine to culture mediums and noted the effect on the growth of various fungi. In general the growth was repressed, the amount of limitation varying somewhat with the amount of hormone and with the different fungi.

A NEW IMMUNOLOGIC REACTION FOR THE DIAGNOSIS OF LYMPHOGRANULOMATOSIS INGUINALIS. F. REISS, Dermat. Wchnschr. **99**:1203 (Sept. 15) 1934.

A mixture of Frei antigen and convalescent serum from a recently cured patient caused a marked increase in reaction as compared with that caused by the Frei antigen alone.

ALLERGIC REACTIONS IN THE MUCOUS MEMBRANES WITH PARTICULAR REFERENCE TO ECZEMA. KÄTE DELBECK, Dermat. Wchnschr. **99**:1229 (Sept. 22) 1934.

In ten persons showing a monovalent sensitiveness of the skin application of the irritating substance to the mucosa caused a definite inflammatory reaction.

A CASE OF CUTANEOUS FIBROMATOSIS WITH SARCOMATOUS DEGENERATION. ERWIN FAHR, Dermat. Wchnschr. **99**:1231 (Sept. 22) 1934.

A case is described in which a fibroma of long standing showed sarcomatous changes though the condition remained localized. TAUSSIG, San Francisco.

PIGMENTATION OF THE SKIN AND SCARLET FEVER. JOACHIM FREY, Deutsche med. Wchnschr. **60**:1204 (Aug. 10) 1934.

A case of uncomplicated scarlet fever in a man aged 28 is reported. The exanthem did not affect the areas of the skin which had been previously sunburned.

PERLSTEIN, Chicago.

THE OCCURRENCE AND TREATMENT OF ECZEMA FROM THE STANDPOINT OF FOCAL INFECTION. ALOIS M. MEMMESHEIMER, Dermat. Ztschr. **70**:1 (Sept.) 1934.

Focal infection plays a much more important part in the development of eczema than is usually believed. Of eighty-eight patients with eczema, seventy-five were found to have foci of infection in the teeth, tonsils, urogenital tract or alimentary canal. Of forty patients with other cutaneous disorders, thirteen had foci of infection. Treatment of eczema was considerably facilitated by the removal of the focus of infection.

THE DURATION OF LIFE OF THE SPIROCHETE OF SYPHILIS IN THE LEECH. R. WAGNER, Dermat. Ztschr. **70**:11 (Sept.) 1934.

Experiments performed by Wagner showed that Spirochaeta pallida lives but a short time (one-half hour or less) in the leech. This indicates that the possibility of conveying syphilis from one person to another through a leech is not to be seriously considered.

CAN THE SPIROCHETE OF SYPHILIS PENETRATE THE BRAIN FROM THE CORNEA IN RABBITS? R. WAGNER, Dermat. Ztschr. **70**:13 (Sept.) 1934.

Several rabbits were given corneal inoculations of material containing the Nicolas strain of spirochetes. After the keratitis had subsided attempts were made to demonstrate the presence of organisms in the brain by means of testicular inoculation of this tissue in other rabbits. The results were negative in every instance.

TEMPORARY PSYCHOSIS DUE TO AN INJECTION OF SALVARSAN. A. AKOWBJAN, Dermat. Ztschr. **70**:31 (Sept.) 1934.

A psychosis developed after the third injection of neoarsphenamine in a course of antisyphilitic treatment. The psychosis lasted for two weeks. There was no evidence of disturbance of the kidneys or of other organs.

TAUSSIG, San Francisco.

TREATMENT OF CUTANEOUS DISEASES WITH PARAFFIN. A. R. KIRICZIŃSKI, E. I. KICZINA and S. A. GLAUBERSOHN, Przegl. dermat. **29**:71 (March) 1934.

The authors have obtained favorable results from the use of melted paraffin in the treatment of alopecia areata, chronic eczema and Raynaud's disease. The affected areas are covered every second day for from thirty to sixty minutes with melted paraffin at a temperature of from 50 to 60 C. The favorable result is explained by

the lasting heat, by the pressure produced by the solidified paraffin and by the increase of the local metabolism in the tissue. The authors also consider the possibility of using this method in the treatment of gonorrheal complications such as epididymitis, arthritis and prostatitis.

BULLOUS ERUPTION OF THE SKIN OF ONE HALF OF THE BODY FOLLOWING INJURY TO THE HEAD. J. STOPCZYŃSKI, Przegl. dermat. **29**:78 (March) 1934.

Stopczyński describes a bullous pemphigus-like eruption of three years' duration in a man aged 47. The eruption started a few days after an injury to the head and was confined since then to one half of the body. The affected region showed distinct hyposensitiveness to touch, pain and temperature. Before the appearance of bullae during the previous three years the patient had suffered from severe headaches. All these facts show the relation of the bullous eruption to the injury sustained by the central nervous system.

ATYPICAL SCLERODERMA (GOUGEROT). J. I. MEHRELENDER, Przegl. dermat. **29**: 114 (March) 1934.

Mehrelender reports the case of a 64 year old woman in whom there developed, besides multiple circumscribed sclerodermic patches, lesions which resembled the rare form of atypical scleroderma described by Gougerot under the name of *la forme liliacée non indurée* and *atrophie brillante*. Histologically the features of scleroderma were found in the infiltrated and noninfiltrated lesions. The basal metabolic rate of the patient was —34. Mehrelender directs attention to the rarity of the occurrence of scleroderma at such an advanced age.

INTRADERMAL TESTS BY EXTRACTS OF THE ENDOCRINE GLANDS. T. CHORĄŻAK and K. ZISCH, Przegl. dermat. **29**:129 (March) 1934.

Chorążak and Zisch carried out intradermal tests by means of extracts of eight different endocrine glands in sixty-seven patients. In sixty there were only negative reactions, and in seven some reactions were positive. Positive reactions were obtained by the extracts of the thyroid and parathyroid glands, hypophysis and graafian follicles. In certain cases the cutaneous reactions were in accord with the results of the functional examination of the corresponding glands and agreed with the clinical symptoms.

The authors believe that the cutaneous tests cannot as yet replace the more exact examination used until now to determine the condition of the glands, although there sometimes exists a correlation between the results of the two forms of examination.

PRURIGO NODULARIS. J. GOĆKOWSKI, Przegl. dermat. **29**:136 (March) 1934.

Gościkowski describes a typical case of prurigo nodularis in a 66 year old man. The disease lasted for forty years and resisted any local therapy. On the extremities, trunk and scrotum there were numerous itching, grayish-white and grayish-brown nodules with a verrucous surface; they varied from the size of a cherry stone to that of half a hazelnut. The antecubital regions were lichenified.

IRREDUCIBLE SEROREACTIONS IN SYPHILIS. ZOFJA JASTRZĘBSKA, Przegl. dermat. **29**:287 (June) 1934.

Among 1,006 patients with symptomless syphilis who were treated systematically Jastrzębska found 56 who seemed to have irreducible positive serologic reactions. In analyzing these cases she found that only 3 of these patients had received systematic and sufficient treatment from the beginning of the infection. Neglect in treatment in the early stages of the disease seems to the author to be, if not the main cause, at least an important factor in the persistence of the positive serologic reaction. A positive serologic reaction occurring after two years of antisyphil-

itic treatment should not be considered as irreducible, for Jastrzębska has seen patients whose positive reactions changed to negative after six years of treatment. The author considers the cause of the resistance of the positive reactions to treatment to be a hidden focus which is not reached by the drugs used.

Porokeratosis Mibelli. K. Kauczyński, Przegl. dermat. **29**:294 (June) 1934.

The author reports a classic case of porokeratosis Mibelli of four years' duration in a 22 year old laborer who had lesions on the dorsum of both hands and feet and on the posterior aspect of the heels. The histologic examination proved the contention of the authors, who believe that the pathologic changes begin in the walls of the sweat ducts. According to Kauczyński this case does not contribute any information as to the etiology and pathogenesis of the disease.

Radiating Telangiectases of the Skin. J. Alkiewicz, Przegl. dermat. **29**: 332 (Sept.) 1934.

Alkiewicz reports the case of a 29 year old woman who for four years had radiating telangiectases on both legs, as described by Edel (*Brit. J. Dermat.* **38**: 112 [March] 1926). The dilated vessels disappeared under the skin in a central area the skin of which was perfectly normal. The largest lesion was 6 by 8 cm.; the smallest, 3 by 2 cm. In spite of lack of preceding or accompanying changes in the skin the telangiectases are considered by the author as secondary to local changes in the deeper vessels, and that opinion is strengthened by the capillaroscopic picture. The disturbance in the function of the hypophysis which was found interferometrically is considered as of secondary importance.

Bloom, New York.

Two Examples of Roentgen Ray Epilation. Masaki Kihara, Hifu-to-Hitsunyo **2**:456 (Oct.) 1934.

Both the cases of roentgen ray epilation reported occurred in young girls, and both resulted from treatment by practicing physicians. In the epilated areas the hair follicles were atrophic, flattened and without evidence of the shafts of hair. Melanin was lessened in amount and gathered together in shoals, part of the granules being apparently extruded into the lumen of the gland and pushed toward the pore and other granules being taken up by chromatophores and transported deep in the tissues toward the deeper blood vessels.

Ultraviolet rays from the air-cooled quartz mercury vapor arc and stimulating ointments (cantharides and zinc oxide) induced a growth of hair about the periphery of the bald spot after about five months of treatment.

Brennan, Chicago.

Studies on Staining of Spirochaeta Pallida, Particularly on the Relation of the Staining to the Preparation of the Slide: I. Influence of Preceding Preparation with Different Fixatives and Mordants on the Staining of Spirochetes and Constituents of the Blood. K. Ono, Lues: Bull. Soc. japon. de syph. **11**:71 (Aug.) 1934.

Rabbit blood was added to an emulsion of rabbit testicle containing Spirochaeta pallida. Smears were made from this mixture and studied in order to ascertain the best staining method. Twenty different fixatives and mordants and thirty-one staining solutions were used. The following observations were made: 1. The staining of spirochetes and blood constituents is dependent on the preparation with fixatives and mordants. 2. The influence of fixatives and mordants does not depend on the chemical constitution of the staining solution. 3. Satisfactory results were obtained by preparing smears with the following substances: alcohol and ether, solution of formaldehyde, hydrogen dioxide, potassium permanganate, alum, ammonium molybdate, potassium dichromate, Müller's fluid (an aqueous solution of 2.5 per cent potassium dichromate and 1 per cent sodium sulphate) and

a solution containing 4 per cent of formaldehyde. Solution of formaldehyde, hydrogen dioxide and potassium permanganate gave the best results. 4. When these three substances were used first the staining reaction of the blood serum, protein and erythrocytes was markedly reduced and the spirochetes showed up by their strong and almost selective absorption of the stain.

STATISTICAL STUDY ON PRIMARY SCLEROSIS (EXPERIENCE DURING THE LAST FIVE YEARS IN THE CLINIC AT TAKAMATSU). M. YANO and T. ENDO, Lues: Bull. Soc. japon. de syph. **11**:142 (Aug.) 1934.

Primary lesions were seen in 112 males and 3 females ranging in age from 19 to 63. Twenty-three patients had gonorrhea also; 9 had phimosis; 5, soft chancre; 2, scabies, and 2, condyloma acuminatum.

The localization of the primary lesions was as follows: in 61 cases in the sulcus coronarius; in 26, in the prepuce; in 8, in the external urethral orifice; in 6, in the frenum of the prepuce; in 6, on the shaft of the penis, and in 4, in the urethra.

A single primary lesion was noted in 100 cases, two lesions in 9 cases, three in 5 cases and four in 1 case.

The Wassermann reaction of the blood was positive in 64 cases. In 28 of 37 cases (75.7 per cent) spirochetes were found by dark-field examination.

In regard to the result of treatment Yano and Endo divide the patients with primary sclerosis into three groups: (1) those quickly cured by means of a small dose of arsphenamine, (2) those cured after the administration of from 3 to 4 Gm. and (3) those hardly cured after receiving from 4 to 5 Gm. of the same preparation.

BLOOM, New York.

BAKERS' ECZEMA. N. C. VAN VONNO, J. STRUYCKEN and P. BONNEVIE, Acta dermat.-venereol. **15**:343 (Aug.) 1934.

The authors discuss the etiology of the disease and report their observations on twenty-eight cases. They cite different kinds of refiners or improvers of flour used by millers and point out that idiosyncrasy to ammonium persulphate is a frequent cause of bakers' eczema. The cutaneous tests employed consisted of patch tests, scratch tests and intracutaneous injections. Among the patients with bakers' eczema 14 per cent showed hypersensitivity to ammonium persulphate; 21 per cent to wheat and 32 per cent to ammonium persulphate and wheat combined, and 32 per cent showed no hypersensitivity to either of the two substances.

SARCOMA IN LUPUS VULGARIS. M. SCHWARZWALD, Acta dermat.-venereol. **15**:365 (Aug.) 1934.

Schwarzwald describes a case of spindle cell sarcoma which developed in a scar of lupus vulgaris. A few months before, biopsy on a specimen taken from the same region showed the presence of carcinoma. The same patient was operated on eleven years before for adenocarcinoma of the uterus. According to the patient's statement she had received frequent treatment with roentgen radiation for four years. Schwarzwald considers overdosage of roentgen radiation an etiologic factor in the production of malignant degeneration.

BENIGN MILIARY LUPOID (BOECK). A. A. STEIN, Acta dermat.-venereol. **15**:386 (Aug.) 1934.

A case of widespread generalized miliary lupoid is described in which tuberculosis of both lungs and of the bronchial and mediastinal glands was simultaneously established. The clinical picture and the biopsy confirmed the diagnosis of miliary lupoid (Boeck). All the reactions to tuberculin (the Pirquet, the Moro and the Mantoux tests) were negative. The anticutin reaction was positive. The negative reaction to tuberculin became positive owing to the allergic condition of the skin

caused by the artificial sensitization. Stein discusses different theories as to the etiology of miliary lupoid and concludes that tuberculosis is the most frequent cause of this disorder.

ETIOLOGY OF THE STRUMOUS BUBO. (TUBERCULOUS INGUINAL ADENITIS SIMULATING LYMPHOGRANULOMA INGUINALE). V. FELDMANN and J. GOUTINE, Acta dermat.-venereol. **15**:398 (Aug.) 1934.

By the term "strumous bubo" the majority of authors understand a slowly developing inguinal adenitis which is accompanied by suppuration and formation of fistulas and is refractory to treatment. The clinical picture is sometimes the same as that of lymphogranuloma inguinale. The etiology, however, may be entirely different. Feldmann and Goutine describe two cases of strumous bubo which clinically resembled lymphogranuloma inguinale but were proved to be of tuberculous origin. In the first case the tuberculous etiology was proved by the results of experiments on animals. An emulsion prepared from the patient's lymphatic glands was injected into two guinea-pigs, and a marked adenopathy developed in the inoculated animals. The swollen glands of the guinea-pigs were extirpated, and an emulsion was made and injected into two other guinea-pigs. All four animals died shortly after, and at autopsy evidence of acute miliary tuberculosis, with tubercle bacilli, was found in most of the organs. In the second case numerous foci of colliquative tuberculosis together with tuberculous arthritis proved the tuberculous etiology of the strumous bubo. In the first case there was also a marked hypersensitivity to different antigens and even to the physiologic solution. According to the authors this polyvalent hypersensitivity is not rare in cases of tuberculosis and should be taken into consideration when the results of the Frei test are interpreted.

Feldmann and Goutine also cite the opinions of some authors who doubt the absolute specificity of the aforementioned test, and they emphasize the necessity of great accuracy in performing the Frei test. They consider tuberculous adenitis as an endogenous reactivation of an old tuberculous process.

ASTRACHAN, New York.

# Society Transactions

## CLEVELAND DERMATOLOGICAL SOCIETY

J. R. Driver, M.D., *Reporter*

*Regular Meeting, Sept. 27, 1934*

R. E. Barney, M.D., *Presiding*

Tuberculosis Colliquativa. Presented by Dr. W. H. Connor.

T. V., a man aged 42, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, has lost 30 pounds (13.6 Kg.) in the last two years. For the past several years he has worked on a farm, and for a number of years before that he had been employed in a fertilizer plant. Two years ago a series of boils appeared over the arms, in the axillae and on the sides of the neck. The patient does not appear acutely ill, and except for persistent crepitant râles in the apex of the left lung, general physical examination revealed no abnormalities.

On the left forearm there are several granulomatous, nodular areas, with ulcers and draining sinuses. Similar lesions are present in the axillae. There are numerous scars of former lesions, including a number on the skin of the neck, which have been present for a number of years. Over the face, chest and back there is a sparse papulopustular eruption. Smears from the pus of one of the lesions revealed numerous wavy fibrils somewhat resembling mycelia, but cultures on sugar-proof mediums were repeatedly negative for fungi. The Wassermann test of the blood was 2 plus. The Kline precipitation test was negative. Examination of the spinal fluid yielded negative results. The intradermal tuberculin test was positive with dilutions up to 1 : 1,000,000. A roentgenogram of the chest revealed increased mottling and markings in the region of the hilus of the left lung. The patient has been given the Gerson salt-free diet and ultraviolet irradiation. Several treatments with roentgen rays have also been given to various areas.

DISCUSSION

Dr. J. A. Gammel: I had the opportunity of following this patient for approximately a year while he was a patient in the outpatient department of the Lakeside Hospital. Numerous cultures were made from the pus from the lesions, but they have never revealed a mycotic infection. Fibrils resembling mycelia were always present in the pus; these, I believe, were elastic fibers. I am of the opinion that the condition is tuberculous.

Dr. H. N. Cole: I agree with Dr. Gammel as regards the diagnosis, and I thank him for the help he has given my co-workers and me in differentiating these structures which resemble mycelia. Clinically I had thought for some time that this was a case of sporotrichosis because of the distribution of the lesions on the arms and the draining sinuses. Because of the type of lesions present, I am of the opinion that the disease is a form of tuberculosis colliquativa.

Dr. R. E. Barney: The scarring in the region of the cervical nodes indicates an old tuberculous infection. Clinically the active lesions on the arms and the eruption on the face and trunk suggest an eruption due to iodide. The diagnosis of tuberculosis associated with iododerma seems justified.

Favus in an American-Born Child. Presented by Dr. W. H. Connor.

S. H., a boy aged 6 years, from the service of Dr. Cole and Dr. Driver at the Cleveland City Hospital, was born of Jewish parents who have always lived

in the United States. There is no history of an infection of the scalp of either of the parents. The boy had been treated with local applications for over one year before he was admitted to the Cleveland City Hospital with a diagnosis of tinea capitis. There are several coin-sized scaly areas on the scalp, with little or no scar formation; clinically these lesions resemble tinea capitis. Study of the hairs by culture and by direct examination showed the disease to be favus. Treatment has consisted of thallium acetate, which was given a few days ago, and of local application of phenyl-mercuric-nitrate ointment.

DISCUSSION

DR. H. N. COLE: The case is interesting because of the rarity of favus in American-born children. Usually patients with this disease have been born in Europe, or their parents have come from Europe or have had the disease.

DR. R. E. BARNEY: The lack of clinical evidence of scarring may be due to the fact that the case is not of long standing.

ULCUS VULVAE ACUTUM, WITH ORAL LESIONS (PERIADENITIS MUCOSA NECROTICA RECURRENS). Presented by DR. H. N. COLE and DR. J. R. DRIVER.

B. S., a girl aged 18, has always been in good health. She had the usual diseases of childhood but has never had any serious illnesses. For the past two years she has had crops of superficial ulcers in the mouth and on the vulva. The lesions are associated with considerable tenderness and some pain. They heal spontaneously in from two to four weeks and are followed a few weeks later by another attack.

General physical examination revealed nothing abnormal. On the inner surface of the right labium majus pudendi there is a pea-sized superficial, punched-out, sharply demarcated ulcer. The base of the ulcer is covered with an adherent grayish-white membrane. There are several small scars from former lesions on the vulva. There are also several small active lesions on the gums, on the soft palate and in the region of the tonsils. Over various areas of the mucous membranes of the mouth are many superficial scars of former lesions. Smears and dark-field examination of material from the ulcers failed to reveal Spirochaeta pallida or Vincent's organism. Smears from the lesion on the vulva showed Bacillus crassus in large numbers.

Treatment has consisted of local application of mild antiseptics and general tonic measures.

DISCUSSION

DR. H. N. COLE: The literature contains a number of reports of cases of this disease in which lesions were present both in the mouth and on the genitalia. B. crassus has also been found in the blood stream.

DR. E. W. NETHERTON: Has anyone reported this type of disease in males?

DR. H. N. COLE: The disease is considered as being present only in females, and it is said to occur usually in virgins.

PSORIASIS AND BASAL CELL CARCINOMA FOLLOWING ROENTGEN THERAPY. Presented by DR. EDWARD STEINBERG, Erie, Pa.

A. W., a man aged 45, has been treated over a period of ten years with roentgen rays and various local applications for psoriasis. His lesions consist of circumscribed areas covered by silvery, whitish scales; some of the lesions on the scalp resemble cement-like patches, and within the past year some of the lesions have presented superficial ulceration and bleeding.

There are dry, scaly, sharply circumscribed lesions on the extensor surfaces of the elbows and knees and on the scalp, and a number of lesions are present on the body. Many of these lesions are sharply marginated and superficially ulcerated and show a tendency to bleed on slight trauma. Some of the lesions show telangiectasia and scar formation where spontaneous healing has resulted.

A slide from biopsy material shows a superficial malignant degeneration of the basal cell type.

Treatment has consisted of roentgen therapy to the areas showing malignant changes, and improvement has been noted.

DISCUSSION

DR. HOWARD T. PHILLIPS, Wheeling, W. Va.: I think that at present it would be impossible to make a diagnosis of psoriasis. All the lesions are apparently superficial epitheliomas, and I question whether the patient ever had psoriasis. I am of the opinion that the lesions are not the result of previous roentgen treatment.

DR. H. J. PARKHURST, Toledo, Ohio: These patches have a threadlike pearly border characteristic of superficial epitheliomas. So far as I can see there are at present no lesions that resemble psoriasis. It has always been my opinion that malignant changes which develop secondary to psoriasis are practically always of the squamous cell type rather than of the superficial basal cell type such as those which this patient exhibits.

DR. R. E. BARNEY: This case is one of the type about which Dr. Hamilton Montgomery has written a great deal. I believe that he recommends surgical intervention as the treatment of choice.

DR. H. N. COLE: This is a case of superficial extensive epitheliomatosis. In regard to therapy, I believe that excision would be an extremely difficult procedure. Dr. Driver and I have seen quite a number of cases of this type, and we have found that superficial endothermy and occasionally treatment with massive doses of carbon dioxide snow give excellent results.

DR. J. EDGAR FISHER: I prefer endothermy for the treatment in this type of case.

DR. HOWARD T. PHILLIPS, Wheeling, W. Va.: Dr. Morgenstern and I have had a patient under treatment for this condition who presents over one hundred lesions. Various methods have been used. Some of the lesions were curetted; others were desiccated; others were treated by cautery. All these methods were found to be equally successful.

DR. EDWARD STEINBERG: I have treated several of these lesions with roentgen rays and find that they respond well to this treatment also.

XERODERMA PIGMENTOSUM WITH MULTIPLE EPITHELIOMAS. Presented by DR. EDWARD STEINBERG, Erie, Pa.

W. R., a man aged 37, had a brother who, at the age of 22, died from a malignant disease resulting from xeroderma pigmentosum. Two other children in the family have not had the disease. The patient states that two maternal uncles had a similar cutaneous condition of a much milder character. When the patient was aged 15 there developed a deeply pigmented and scaly condition of the skin with ectropion of the eyelids. When he was 16 years old there developed an ulceration on the forehead which has been apparently successfully treated by electrolysis.

On the exposed parts of the body, i. e., on the face, neck, hands and arms, there is a deeply pigmented, freckle-like condition with development of keratoses and atrophy of the skin; there are numerous crusted, ulcerated lesions on the face and ears and numerous keratotic, verruca-like patches over the skin of the cheeks and forehead. There is a palm-sized area on the interscapular area of the back showing superficial ulceration and bleeding. The disease has produced destruction of the cartilage of the nostrils as well as considerable destruction of the cartilage of the left ear.

A report on a biopsy states that the lesions are of a basal cell character.

Some improvement has been noted on several lesions treated with fractional doses of roentgen rays.

DISCUSSION

DR. J. R. DRIVER: The extent of malignant degeneration present in this case is unusual, and I am interested in the fact that the pathologic picture is stated to be that of basal cell epithelioma. In my experience malignant degeneration in cases of xeroderma pigmentosum has always been of the squamous cell type. I should like to see further biopsy specimens.

DR. H. N. COLE: It is unusual to see xeroderma pigmentosum in a person as old as this patient. Patients with that disease usually die earlier.

IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA OF KAPOSI (?). Presented by DR. EDWARD STEINBERG, Erie, Pa.

T. R., a man aged 49, for the past nine months has complained of shortness of breath, cough with expectoration of considerable whitish sputum, headaches and weakening of the legs; he also states that he sleeps poorly. The patient has become progressively weaker and has lost about 15 pounds (6.8 Kg.) in weight. About four months ago a small nodule developed on the right side of the face; this has gradually increased until now it is the size of a pigeon egg. About twenty other lesions of similar character and somewhat smaller have developed on the sides of the face, neck, chest, back and thighs. The skin of most of the lesions is freely movable over the surface and is the color of approximately normal skin; other lesions have a bluish or purplish-red tinge, and a few present vesicles on the surface which are firm and do not appear encapsulated. The lesions are freely movable. They appear to be subcutaneous at the start; later they involve the overlying skin and are not tender or painful. There are no subjective symptoms. Aside from drugs used for the treatment of asthma, no medication has been used.

The Wassermann and microscopic precipitation tests of the blood were negative. Examination of the urine showed no albumin or sugar. The results of the differential blood count were essentially normal.

A biopsy made by Dr. H. H. Bullard of Erie, Pa., on Aug. 22, 1934, was reported on as follows: "The sections show the connective tissue layer of the skin to be greatly thickened. The epidermis shows but slight hyperplasia. A considerable part of the connective tissue layer of the skin is of normal white fibrous connective tissue structure. The connective tissue bundles, however, are for the most part widely separated by large numbers of cells which do not form part of the normal skin. These cells show a tendency to be most numerous around the sweat glands in the skin. They are not confined to this situation. The cells in these accumulations consist of many polymorphonuclear leukocytes, moderate numbers of eosinophilic polymorphonuclear leukocytes, moderate numbers of lymphocytes and plasma cells and many swollen endothelial cells. These swollen endothelial cells appear to be the cells of the capillaries of the skin. Many oval or spindle-shaped cells appear edematous, while others show foamy reticular cytoplasm. Apparently these cells are the connective tissue cells of the skin which have become edematous and show perhaps other degenerative changes. A considerable proportion of the cells in the cellular accumulation are difficult to identify, but on the whole the lesion appears to be due to an acute and subacute inflammatory reaction together with edema and poorly defined degenerative changes. Careful examination fails to reveal definite evidence of neoplastic growth. The thickening of the true skin is undoubtedly due to the edema and to the presence of the cells described. Mitotic figures are not observed. The diagnosis: marked acute and subacute inflammatory reaction together with edema and degenerative changes as described. The specimen does not appear neoplastic."

A biopsy made by Dr. Charles F. Geschickter of Johns Hopkins University, Baltimore, on Aug. 30, 1934, was reported on as follows: "I believe that the disease is Kaposi's sarcoma. The original sections which I examined were somewhat thick and suggested that condition, but because of the predominant compact stroma, I thought that myoma cutis was a good provisional diagnosis."

DISCUSSION

DR. H. N. COLE: It is unfortunate that the microscopic slide presented was not well stained or well prepared. It is unusually thick, and it is difficult to determine the exact structure of the tumor. However, from what I can make out its structure does not resemble the picture of Kaposi's sarcoma, and I am under the impression that the nodule is not a malignant growth. From what I could see, I should be more in favor of a diagnosis of sarcoid-like structure. Clinically the lesions do not have a tendency to break down, and they resemble more the Darier type of sarcoid. There is apparently no involvement of the bones, but roentgenograms should be made. Also, it would be interesting to see whether there are any pathologic changes in the chest and any evidence of tuberculosis. Tuberculin tests should be made also. So far as sarcoma of Kaposi is concerned, there are no clinical signs to suggest such a diagnosis.

DR. J. EDGAR FISHER: The absence of lesions on areas in which Kaposi's sarcoma usually occurs and the short duration seem to rule out this diagnosis. The patient says that he has taken atropine, and the possibility of an eruption due to a drug should be considered.

DR. R. E. BARNEY: The possibility of an eruption due to iodine should perhaps be considered. At any rate, if it were possible for Dr. Steinberg to obtain more sections for examination, the matter might be clarified.

DR. EDWARD STEINBERG, Erie, Pa.: I shall try to get more material for biopsy, but the patient has refused to have any more made.

NOTE. At the February meeting of the Cleveland Dermatological Society Dr. Steinberg reported that, acting on the suggestion that the condition might be sarcoid, he had administered three injections of neoarsphenamine at intervals of five days and that there was approximately a 75 per cent improvement in the lesions. Dr. Steinberg also reported that roentgenograms of the long bones and pelvis showed no abnormalities. Intradermal tuberculin tests were negative with dilutions of from 1 : 1,000,000 to 1 : 1,000. A week after the administration of neoarsphenamine was discontinued the patient had hemorrhages from the lungs and died. At autopsy lesions similar to those found on the skin were found in the lungs, in the pancreas and in the mesentery. Specimens taken for biopsy were examined by Dr. Fred D. Weidman and Dr. Joseph McFarland, both of Philadelphia, and by Dr. James Ewing, of New York. The report by Dr. Fred D. Weidman is as follows: "In the center of the section the epidermis shows a mild grade of acanthosis. The changes there appear not to be related, except secondarily, to the changes deeper down in the corium. In the corium there is a nodule about 4 mm. in diameter extending from the pars papillaris to the subcutaneous tissue. It is not encapsulated; strands of its substance extend in an infiltrative way in all directions peripherally. Within the nodule, smaller and larger remnants of the original collagenous matrix still remain. These are of varying kinds. They are dissected to a varying extent by the pathologic cells. Such cells are of varying kinds. Thus a small number of lymphocytes are found at places around the blood vessels and are clearly part of a secondary reaction; i. e., they are not a part of the fundamental pathologic changes. The predominating pathologic cell is a large spindle cell with a large hyperchromatic nucleus. This cell commonly occurs individually or in small short bundles. In the latter case newly formed capillaries are commonly associated, the long dimension of which extends parallel with that of the bundle concerned. Such bundles interlace or even whorl in the fashion of a fibrosarcoma. The second type of cell is much larger, sometimes rounded, but more often polygonal or almost stellate. It is sometimes multinucleate and frequently contains an indefinitely outlined vacuole. The vacuole may in turn contain pink granular material or polymorphonuclears or fragments of cellular detritus. At times it is impossible to trace a connection between these cells, both multinucleate and spindle, and collagen bundles as well as between such cells and highly hyperplastic ones of the capillary linings.

"In no case do any of the pathologic cells occur in notably large masses, it appears rather as though the hyperplasia had been been lighted up rather generally and diffusely throughout the entire lesion.

"The sweat glands included within the lesion are atrophic. Those on the outside are highly developed and exhibit a marked edematous infiltration of the interstitial substance. A few small hair follicles are included in the section, and these appear to be normal. The subcutaneous tissue appears to be normal.

"By way of summary it may be said that the nodule is fairly well circumscribed and consists of neoplastic cells which appear to originate both in the nuclei of the collagen bundles and the lining endothelium of the capillaries. The cells as well as their nuclei are of such embryonal type that I feel compelled to regard them as neoplastic rather than granulomatous, at least on a morphologic basis. Part of these features (participation of endothelium) conform to those of Kaposi's sarcoma, but the hemorrhagic areas and pigmentation are utterly lacking. There is no tendency toward hemorrhage. Under the circumstances, I feel constrained to go no further than making a diagnosis of fibro-endothelioma. The vacuoles within the multinucleated cells conceivably represent the lumens of capillaries the surrounding and hyperplastic endothelial cells of which have not proceeded so far as to separation of the cytoplasms one from the other."

Dr. Joseph McFarland of Philadelphia, did not agree with Dr. Weidman and Dr. Geschickter. He believed that the condition was granulomatous.

Dr. James Ewing of New York, said: "In this remarkable case I am not able to reach a positive diagnosis as to the origin of the tumor. In one of the pleural sections there is a clear, distinctly carcinomatous area which suggests a primary tumor of the lung. The description of the root of the lung also suggests a carcinoma of the lung, rapidly extending to the hilus and pleura. Cutaneous metastases are common in cases of pulmonary carcinoma. Kaposi's sarcoma never produces this general picture."

DISCUSSION

Dr. H. N. Cole: I have examined some of these subsequently made sections, and while I do not profess to be a pathologist, in one section I note that the cellular infiltration in the corium is separated with septums of connective tissue, a picture one sometimes finds in cases of sarcoid. It is remarkable, however, that the patient responded so well to three injections of neoarsphenamine. I am still somewhat in doubt, but I believe that the case may be one of sarcoid; lesions in the lungs are sometimes seen in such cases.

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## LOS ANGELES DERMATOLOGICAL SOCIETY

Nelson Paul Anderson, M.D., *Secretary*

*Regular Monthly Meeting, Dec. 11, 1934*

Moses Scholtz, M.D., *in the Chair*

Eruption Due to Bromide or Iodide? Presented by Dr. Saul S. Robinson.

T. R., a Hungarian housewife aged 48, has had a generalized eruption with involvement of the eyes for five years. She says that she has not used either iodides or bromides. She has taken solution of potassium arsenite for the past two years as this was the only medicine which gave her relief.

On the right forearm is a round, nickel-sized, elevated, well defined bullous lesion. On the upper and lower extremities and on the face and neck are erythematous and white areas of scarring and atrophy at the site of old bullous lesions. The provocative Wassermann test of the blood was negative. A blood culture made on March 27, 1933, and cultures of fluid from the bullae did not

show pathogenic organisms. The patient was presented at a meeting of this society in January 1933.

DISCUSSION

DR. NELSON PAUL ANDERSON: When this patient was presented in 1933, the members more or less agreed that the condition was a granulomatous eruption belonging to the bromoderma group. I see no reason to change that opinion. The fact that solution of potassium arsenite gives relief strengthens my suspicion that the eruption is an ioderma or bromoderma.

DR. MOSES SCHOLTZ: Is it not strange that a bromoderma should exist for five years?

DR. H. C. LINDSAY: The lesions are much like those of a dermatitis factitia in which there is some granulation.

DR. H. S. CAMPBELL: The last time I saw the patient I agreed that the disorder was either a bromoderma or an ioderma. However, it seems incomprehensible that an eruption due to a drug should persist for a year or more when there is no ingestion of that drug. Furthermore, the areas of flat wide superficial scarring located solely on the forearms and lower portion of the legs lead me at present to consider the diagnosis of dermatitis factitia.

DR. G. F. KOETTER: Dr. Chambers, Dr. Olson and I have watched this patient carefully in an effort to discover evidence of a factitious element, and we felt that we had ruled out the possibility of dermatitis factitia. After injection of 0.3 Gm. of neoarsphenamine for a provocative Wassermann test, numerous bullae developed. There was no intake of bromides or iodides while the patient was in the hospital. I suggest that a Pels-Macht test be made. While the patient was under our observation all the lesions began as bullae and healed with a circular, depressed cicatrix.

DR. SAUL S. ROBINSON: A biopsy was made two years ago when I first saw the patient. Chronic inflammatory changes were noted in the lesion.

DR. SAMUEL AYRES JR.: Do these lesions disappear spontaneously?

DR. SAUL S. ROBINSON: They disappear when the patient takes solution of potassium arsenite.

DR. H. S. CAMPBELL: I understood her to say that in the past five years the eruption has practically disappeared at various times, only one lesion remaining, as is the case at present. The whole course is rather suggestive.

DR. MOSES SCHOLTZ: I never heard that arsenic had any effect in clearing up bromoderma or ioderma.

DR. H. C. L. LINSAY: There are no lesions on the back. I think that the patient has a dermatitis factitia.

A CASE FOR DIAGNOSIS. Presented by DR. SAMUEL AYRES JR.

B. R. is a schoolgirl aged 16. The family history gives no record of any cutaneous disease except that in a sister, one year younger than the patient, a similar eruption has begun to develop during the past three months. The patient's illness began one and a half years ago, and the eruption was first noticed on the back of the neck. The lower part of the chest has become involved during the past two months.

The eruption is limited to the back of the neck, the upper part of the back and the sides of the neck and chest. The eruption is ill defined and consists of a somewhat mottled, dirty-looking, gray-brown pigmentation; in places, especially over the lower part of the chest, it shows a somewhat adherent fine scaling. Some of the newer lesions, such as the ones on the chest, appear as discrete and confluent pea-sized brownish-buff macules. On the sides of the neck and over the clavicles there are white atrophic-appearing macules which are definitely depressed. The patient's sister has similar lesions on the chest only.

Scrapings from the more recently involved areas on the chest examined today under 40 per cent potassium hydroxide failed to reveal Microsporon furfur or other fungi. At least three previous examinations have given negative results.

Various ointments, including Whitfield's ointment and ointments containing sulphur, etc., have been used for over a year without benefit.

DISCUSSION

DR. H. C. L. LINDSAY: I believe that the condition is a pseudoleukoderma colli due to a fungus.

DR. SAMUEL AYRES JR.: This case has troubled me a great deal. The patient has been treated by different physicians at the Los Angeles County Hospital for one and a half years. I first thought that the eruption was due to tinea versicolor, although there appeared to be a certain amount of macular atrophy in the lesions of the neck. The location of the eruption and the form of the lesions, discrete macules with scaling, pointed to the probability of its being due to tinea versicolor. Many scrapings have been made, and no fungi were found. As far as acromia parasitica is concerned, I have always associated that condition with pityriasis alba. My conception of the latter disease is that it causes a dry lesion with whitish scaling due to some microbic infection which interferes with normal tanning of the skin, but I do not recall having seen any atrophy in those lesions. That is apparently different from the pea-sized patches exhibited by this patient. The fact that a similar eruption appeared on the skin of the patient's sister strengthens the probability that the disorder is a parasitic condition.

DR. H. C. L. LINDSAY: Castellani mentioned one or two forms of fungi causing parasitic achromia, but there are a great many more than he mentions in his article. Several books list other fungi as causing parasitic achromia. Even in cases of pityriasis versicolor there is no true vitiligo lesion but rather an increased pigmentation due to fungi surrounding the areas that are free from pigment and fungus.

ACNITIS, ACNE VARIOLIFORMIS, SCLERODERMA. Presented by DR. H. C. L. LINDSAY.

I. B., a nurse aged 34, was born in England. She has been ill for nine years. In 1918 she had scarlet fever, temporary albuminuria and otitis media. Later alopecia areata developed, but the hair grew again. She then had lupus erythematosus involving the scalp; the latter condition was apparently caused by foci of infection in the teeth. Later a butterfly eruption developed over the bridge of the nose. As time went on a vasomotor disturbance of fingers with alternate blanching and congestion of the skin appeared. Finally an acute polyarthritis deformans developed; this was treated by removing the tonsils and extracting the devitalized teeth. The patient was married in 1923; she became pregnant, and during pregnancy rigidity and stiffness of the skin and pain and stiffness of all the joints developed. The skin became bronzed and leathery (scleroderma). The patient was told that she had Addison's disease and an endocrine disturbance. Improvement followed the taking of thyroid, parathyroid and ovarian extracts. The pregnancy ended in a normal delivery at term. The patient nursed the baby for six months, and the condition of the skin became worse. Pyelitis developed shortly after delivery and was followed by total alopecia. The arthritis continued; the patient became emaciated, and crippling and atrophy of the extremities developed. The skin became stiff, and papery white patches appeared on the arms and legs. A marked edema of the lower extremities developed. When the hair began to grow again the patient applied a hair dye, which gave her a violent dermatitis. She then received five injections of gold and sodium thiosulphate, which aggravated the hyperemic condition of the toes but improved the disorder of the skin in other parts of the body.

The patient looks prematurely old. The face is pitted with atrophic scars of acne varioliformis, and on the head and arms are lesions of acnitis. She has sclerodermatous lesions on the scalp and fingers. She is nervous and appears ill but animated. When lupus erythematosus first developed the patient was seen by

Dr. Howard Fox, who confirmed the diagnosis of lupus erythematosus of the scalp. Later she was seen by Dr. Ormsby, who made a diagnosis of scleroderma on some lesions. The Wassermann reaction has always been negative. A biopsy has not been made. Ultraviolet radiation was used on the alopecia with good results. Gold sodium thiosulphate was given to the patient in Portland and the results were beneficial, as a whole. The removal of the foci of infection brought about a cure of the alopecia areata.

DISCUSSION

DR. SAMUEL AYRES JR.: The patient also has an acute dermatitis which looks like a dermatitis medicamentosa and developed after a test with iodine was made on the gallbladder.

DR. H. C. L. LINDSAY: I saw this patient in 1919. At that time the only symptom she presented consisted of lesions on the scalp. She was a nurse in the Vancouver General Hospital at that time. The lesions of the scalp were typical of lupus erythematosus. They had a typical raised border and follicular plugs with some scaling. The history shows that the patient had recurrent exacerbations of alopecia areata followed by regrowth of hair. Later she became pregnant, and chloasma developed. The entire history is interesting. She also has scleroderma, as pointed out in the history and as evident from some of the lesions which are present now.

LICHEN PLANUS HYPERTROPHICUS OR KAPOSI'S SARCOMA? Presented by DR. NELSON PAUL ANDERSON.

M. C., a widow aged 66, presented herself on Nov. 27, 1934, with an itching disorder of from six to seven months' duration which affected both feet. She had first noticed a lesion on the right ankle and consulted a physician who treated her for varicose veins with injections and ultraviolet irradiation. The latter therapy inhibited the itching temporarily. The condition began as a small red itching discoloration and slowly evolved to its present state, which consists of four violaceous, circumscribed, elevated and lichenified patches on both feet, about the instep, ankle and heel. Laboratory examinations have included a Wassermann and a Kahn test, both of which were negative.

A specimen for biopsy was taken from the surface of the skin of the right ankle. Sections from different portions of the tissue revealed a thickened hyperplastic covering of stratified squamous epithelium, beneath which were some glandular structures and an occasional duct embedded in fibrous tissue of cutis and subcutis. The epidermis showed some hyperkeratosis and scaling. The rete cones and interpapillary processes showed irregularity in size and shape and in the distance to which they extended into the underlying cutis. The cutis adjacent to the basal layer showed considerable inflammatory involvement, as evidenced by a lymphocytic infiltration and a small round cell infiltration. In this region were a few small capillaries showing some extravasation of red blood cells. Also in the same region were a few small irregular pigmented areas due to effusion of blood, which accounted for the discoloration of the skin.

DISCUSSION

DR. H. S. CAMPBELL: I wish to subscribe to the diagnosis of lichen planus hypertrophicus. The striae are particularly characteristic and well marked.

MELANOSARCOMA OR NEUROFIBROMATOSIS? Presented by DR. STANLEY CHAMBERS.

P. S. A., a man aged 41, says that in October 1918 he was thrown by an explosion of a shell and fell on the right buttock and lower lumbar region. Shortly thereafter pigmented areas developed in the lower lumbar region and thighs. Later tumors developed in the pigmented areas. In the past ten years the patient has had attacks of severe pain in the lower right part of the back and in the thigh. Recently the pain has been more severe. About the middle of April 1934 there

developed swelling in the right inguinal region, and in November the patient became conscious of severe pain in the right groin. He was then hospitalized by a physician, who removed a tumor from the right inguinal region and one from the right hip in the neighborhood of the iliac crest. The patient states that on Nov. 20, 1934, or thereabouts he noticed new lesions appearing in the involved areas. These appeared with considerable rapidity and were of an entirely different color, e. g., blue and black. There was associated pain. The tissue removed was examined, and the histologic structure proved to be that of melanosarcoma.

The patient presents a typical case of Recklinghausen's disease, the condition being confined chiefly to the lower part of the trunk and to the hips and thighs. There are a few scattered pigmented lesions over the lower part of the legs and arms. There are two healed surgical incisions, one in the right loin and one above the right crest of the ileum, the sites from which nodular tumors were removed. Scattered among the pigmented lesions of Recklinghausen's disease are numerous dark purple areas characteristic of melanosarcoma.

Microscopic section of a removed lymph node revealed that all the normal structures had been replaced by a new growth made up of hyperchromatic spindle cells varying in size and shape. There were many large nucleated and multinucleated giant cells of the tumor variety. A large number of cells contained brownish-black pigment. Many cells contained so much pigment as to completely obscure the cell markings. Many mitotic figures were noted.

DISCUSSION

DR. W. H. GOECKERMANN: I do not know of any records that show the frequency with which the lesions of Recklinghausen's disease become malignant. I have seen several hundred such cases, but I do not recall any in which the condition became malignant, though it is known that the life expectancy of patients with Recklinghausen's disease is not great. Nevertheless, it would be interesting to ascertain the tendency of these lesions to malignant degeneration. There is not the slightest doubt that the microscopic picture shows a vicious process.

TRAUMATIC ULCER ON THE BASIS OF DEFECTIVE ARTERIAL CIRCULATION PLUS SECONDARY PYOGENIC AND SAPROPHYTIC INFECTION. Presented by DR. MOSES SCHOLTZ.

A. W., a man aged 76, has an irrelevant family history. When the patient was 9 months old his toes were burned off by fire. He has a sore on the foot of four years' duration. This started after he pared a callous spot on the sole of the foot.

There is at the aforementioned site an irregularly shaped, palm-sized superficial ulcer, not infiltrated or raised, with sharply scalloped edges, surrounded by a dusky red hyperemic zone. The base of the ulcer shows a yellow-red granulating surface of boggy consistency exuding a seropurulent discharge in the center. In places there are scant dirty, blackish deposits. The patient also suffers from enlargement of the prostate and frequency of urination. Roentgenograms of the bones of the feet showed no abnormalities, and the Wassermann reaction has been negative. Treatment has consisted of ultraviolet irradiation and local application of solution of potassium permanganate.

DR. H. S. CAMPBELL: The patient presents a picture of shallow chronic ulceration which recently has somewhat improved under local therapy. I should attempt to cleanse the surface with saline solution and stimulate granulation. Healing would be hastened by Thiersch grafting. The literature, I believe, has several references to the changes created by these chronic ulcerations simulating malignancy. I wish to draw the attention of the members to the fact that Dr. Scholtz and I were given the diagnosis of carcinoma on tissue in a case which later proved to be one of factitious dermatitis. These reports were made on material taken from the margins of the same lesion by two expert pathologists. I have other similar reports on lesions which eventually proved to be either simple or fungous ulcerations. It is therefore a serious matter when one is forced to depend on biopsy alone in these cases.

DR. MOSES SCHOLTZ: The patient has had this ulcer of the sole for four years. My diagnosis is that of traumatic ulcer resulting from defective arterial circulation. I believe that syphilis can be ruled out on the basis of the clinical appearance of the lesion. The ulcer shows a partial improvement under application of packs moistened with potassium permanganate and ultraviolet irradiation. I think that Dr. Morrow of San Francisco calls this condition dysmoma.

NODULAR SUBEPIDERMAL FIBROSIS (MICHELSON). Presented by DR. SAMUEL AYRES JR.

F. W., a woman aged 44, states that the duration of her present illness is seven years and that lesions first appeared on the right forearm. Other lesions have since appeared on the arms, shoulders and legs. The lesions begin as a tiny, hard, subepidermal nodule which slowly enlarges and ultimately results in a tiny depressed cicatrix-like area, which, however, retains a hard, deep infiltration. None of the lesions have ulcerated, although several have been removed for biopsy and the resulting wounds have been slow to heal. None have ever disappeared spontaneously. The patient is otherwise well, although rather obese. Dermatologic examination shows about a dozen lesions scattered on the arms and on the back of the shoulders and shins. The patient states that the upper lesion on the right forearm is the oldest and appeared about seven years ago. This lesion consists of a nodule about the size of a cherry seed; it is mostly subepidermal and on palpation has a sclerotic button-like feel; in the center there is a certain depressed scarlike appearance surrounding an oval, slightly elevated, brownish, somewhat verrucous nodule. The other lesions are similar in appearance. There is a healing wound on the left arm left by the removal of tissue for biopsy. On the left shin is a pea-sized brownish violaceous hard nodule, a good deal of which is subepidermal. The lesions are freely movable. Wassermann and Kahn tests were negative on May 19, 1933.

Examination of a biopsy specimen showed hyperplasia of the squamous epithelium and marked cornification. There were a few nests of epithelium in the tissues which appeared somewhat suggestive of an early stage of malignant degeneration.

DISCUSSION

DR. SAMUEL AYRES JR.: Michelson has written an article on this subject recently. The entity has been described in the French literature and elsewhere, but not in any comprehensive manner. Michelson went into considerable detail regarding the histologic changes. The lesion begins as an inflammatory condition which, instead of going on to formation of pus, undergoes cicatricial changes analogous to those occurring in keloid. He emphasized the changes in the connective tissue, in which there is considerable hypertrophy of the collagen bundles, which later exhibit a sort of homogenization. In this case the most striking change is in the epithelium, which is greatly hypertrophied. Characteristic changes in the connective tissue are also present, however. The only treatment apparently is excision. I have never seen a patient with as many lesions as this woman has.

DR. MOSES SCHOLTZ: I do not quite understand the name, as every fibroma is always subepidermal and nodular.

DR. SAMUEL AYRES JR.: This condition is different from an ordinary fibroma. The ordinary fibroma is elevated.

DR. W. H. GOECKERMAN: In the earlier years of my experience much interest was shown in these fibrotic infiltrations, chiefly because of a lack of familiarity with the sarcoids. When biopsy material was sent to the general pathologist he often raised the question of malignancy, but the lesions are commonly seen and are always benign. Their course never follows that of a true sarcoid.

ICHTHYOSIS OF BODY. TINEA OF SCALP? Presented by DR. SAMUEL AYRES JR.

E. F., a boy aged 13, has a disorder of the scalp which has been present all his life. The skin has always been dry, and he has used various local medication

without much benefit. The basal metabolic rate is —5. There is a profuse scaling of the scalp extending down into the ears. The hair is thin, and the scalp presents a definite atrophic appearance. No broken hairs are seen. Microscopic examination of scales and hairs revealed no definite fungi. A culture on Sabouraud's medium showed the presence of an unidentified fungus.

DISCUSSION

DR. SAMUEL AYRES JR.: This boy was referred from the State School for Delinquents because of the fear that the condition might be infectious. He has a dry, apparently ichthyotic skin. When I saw him about a week ago there was a good deal more dry scaling than there is now, although no typical scutula as one sees in favus were observed. There were a few hair stumps, and there was marked thinning of the hair. The scaling extends into the auditory canals and nostrils like a seborrheic dermatitis, and yet the condition of the scalp suggests a sort of tinea. I was not sure whether I could see any fungi under the microscope. Some cultures were made, and they showed a fungous growth, which, my technician thinks, belongs to the favus group. The patient states that his parents and one sister have never been affected.

NOTE.—The organism obtained on culture subsequently proved to be Alternaria.

DR. H. S. CAMPBELL: I have seen quite a number of cases of favus involving the scalp, both in marked and in mild degree. The scutula, color and odor are unmistakable clinically. There is no doubt that this patient's disorder is not favus, as Achorion Schönleinii leaves unmistakable traces. I have seen a condition somewhat similar to that of this boy in a patient who was presented with the dual diagnosis of ichthyosis and seborrhea.

DR. W. H. GOECKERMAN: I wish to make a diagnosis of congenital abnormality of the hair. I think that these partial ectodermal defects are not uncommon, and I should be willing to believe the boy's statement that he has had the condition since birth.

DR. CHARLES CASKEY: I am also of the opinion that the process responsible for the ichthyotic skin is the one operating on the scalp too.

DR. SAMUEL AYRES JR.: My diagnosis likewise is that of an ichthyotic congenital defect associated with seborrheic dermatitis. About a week after I sent in the report on the culture the fungus began to grow from the hairs I had plucked. My co-workers and I have seen two cases of typical favus recently. Certainly there is no evidence of either the characteristic odor or scutula which were present in these two cases.

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## NEW ENGLAND DERMATOLOGICAL SOCIETY

J. HARPER BLAISDELL, M.D., *Secretary*

*Dec. 12, 1934*

RUDOLPH JACOBY, M.D., *President*

GUMMAS OF THE RIGHT TIBIA. Presented by DR. HENRY BENJAMIN, Medford, Mass.

This man, a painter aged 63, states that about five months ago his right leg was hit with a board which bruised his shin. A lesion developed and steadily increased in size until it reached that of a 50 cent piece. Within a short time two other lesions appeared below the original one. A burning sensation is present occasionally.

There are three circular ulcers on the middle third of the right leg, varying in size from that of a 25 cent piece to that of a 50 cent piece. The uppermost

ulcer is hard and has raised edges; the others appear punched out in the skin. The base of each ulcer is covered with a greenish cheesy slough. A diffuse erythematous zone around the leg extends from about 2 inches (5 cm.) below the knee to the ankle. Varicose veins are present below the knee. The patient also has several thin scars about 1 inch (2.5 cm.) long scattered over the body.

Three Kahn tests made during the last two months were negative. Roentgenograms of the tibia taken in the anterior posterior position showed no abnormalities. Those taken in the lateral position showed a slight bowing of the anterior border of the tibia, with thickening of the cortex, and a slight irregularity ot the periosteal contour suggested periostitis.

The patient has received 15 grains (0.972 Gm.) of potassium iodide three times a day and local treatment with ointment of boric acid. No change in the condition has been noted.

DISCUSSION

DR. J. HARPER BLAISDELL, Boston: I suggest a diagnosis of "liquor leg." The patient takes about ten drinks of whisky a day, and beer he does not count. The Wassermann reaction was negative on three occasions.

DR. WILLIAM P. BOARDMAN, Boston: When the Wassermann test was first used the late Dr. Nichols brought me several specimens of blood from patients with syphilis of the bones, and I obtained uniformly negative results on them. Papers appeared shortly after that which showed how frequently negative reactions are obtained in late cases of periosteal thickening, a condition often accompanied by ulcers of the leg. The sharply cut circular unilateral ulcers and the scars on this patient are rather typical of syphilis. In such cases roentgen examination almost invariably shows changes in the periosteum, and in this case such changes are evident in roentgenograms taken in the lateral position but not in those taken in the anteroposterior position. In regard to the treatment of these ulcers, my co-workers and I have had two patients with similar conditions in the ward; the skin was shiny and red and the circulation poor; the condition improved to a certain extent when the leg was elevated and antisyphilitic treatment was instituted, but the degree of improvement was slight. In these two cases a graft was performed and fairly good results were obtained. These conditions are often circulatory as well as syphilitic in origin.

DR. WILLIAM J. MACDONALD, Boston: Regarding the difficulty of bringing about the healing of ulcers, I do not know whether the members have read the report of Dr. Everitt Lane of Oklahoma City. He uses an adhesive elastic plaster. There is a special technic of application. He emphasizes the number of cures he obtains in cases of chronic ulcers of the leg.

DR. FRANCIS M. THURMON, Boston: In the treatment of chronic ulcers, good results are obtained with local applications of a 5 per cent aqueous solution of gentian violet.

DR. HENRY BENJAMIN, Medford, Mass.: In regard to the circulation in the affected area, there is good pulsation over the dorsalis pedis artery in each foot. The circulation seems to be well established.

DR. AUSTIN W. CHEEVER, Boston: I do not doubt that the man has syphilis and an old periostitis, but I do wonder whether the ulcers are syphilitic. There is no pigmentation, no dusky cyanotic hue around them, such as is usually present around old syphilitic ulcers. I believe that the condition may be a symbiotic reaction due to an old syphilitic infection in a patient with a history of excessive ingestion of alcohol.

HIDRADENITIS. Presented by DR. HENRY BENJAMIN, Medford, Mass.

This woman, aged 22, complains of lumps in the axillae which have increased in size during the last six months. The masses have never disappeared entirely, have never grown larger than the size of a dime and are painful. A follicular eruption has been present during the same period.

The hair follicles in both axillae are inflamed and prominent. Beneath them are enlarged and tender glandular masses from 5 to 10 mm. long.

The patient has received treatment with compound calamine lotion.

DISCUSSION

DR. WILLIAM J. MACDONALD, Boston: I asked that this case be discussed, not because I doubt the correctness of the diagnosis but because I am wondering what will be done in the way of treatment. I suggest prompt curettage of the lesions followed by treatment with fractional doses of roentgen rays.

DR. RUDOLPH JACOBY, Boston: The patient says that she has no trouble except when sweating, at which time she notices an enlargement of the glands in the axillae. These glands then become larger and painful, and she has trouble in raising the arm. It occurred to me that the use of a 20 or 25 per cent solution of aluminum chloride, carefully used, may help.

PEMPHIGUS. Presented by DR. JOHN G. DOWNING, Boston.

This woman, aged 26, states that in April 1934 she first noticed water blisters appearing in the axillae; these rapidly broke and healed without scarring. Five months ago the eruption spread over the back, chest and face and sores appeared in the mouth. The lesions appeared as papules which became vesicular and then bullous. There was some itching when the lesions broke out.

There are large bullous and vesicular lesions of superficial skin, each lesion being surrounded by an area of slight induration. There are crusted lesions over the scalp and face, bullous and vesicular lesions in a bathing suit distribution on the body and fewer lesions on the extremities.

Examination of the urine and the Kahn test gave negative results. The blood showed slight anemia and leukocytosis.

The patient has received gentian violet therapy externally and has followed a diet with high vitamin content and taken methylthionine chloride U. S. P. (methylene blue) without much result. Because of smoothness of the tongue she has received liver extract, 5 cc. daily, and marked improvement has been noted since the last type of treatment was instituted.

DISCUSSION

DR. J. HARPER BLAISDELL, Boston: I am surprised to hear pemphigus on the face mentioned. This patient has a severe seborrheic dermatitis of the face, chest and back.

DR. J. L. GRUND, Boston: There is a question as to whether or not the entity referred to as the Senear-Usher type of pemphigus exists. Wise claims that cases placed in the latter category are really cases of bullous forms of lupus erythematosus.

DR. J. HARPER BLAISDELL, Boston: On places on the back, Dr. Towle and I could pick off some of the skin. It is rather unusual to see an Irish girl aged 26 with pemphigus, but that does not rule out the diagnosis.

DR. E. LAWRENCE OLIVER, Boston: I saw a case much like this one at the Long Island Hospital. At times the lesions looked much like those of lupus erythematosus. I think that is how the eruption began, and then bullous lesions appeared. At other times the eruption looked like severe erythema multiforme. I think that all three diagnoses could have been made. The patient seemed to have a mixture of the three diseases. Whether such cases are all cases of true pemphigus, I cannot tell. I suggest that the Pels test be made. Pels says that dermatitis herpetiformis may cause a positive reaction to his test. If that is true the test is not of as great help as it was believed to be. Clinically I think this case is pemphigus with a seborrheic condition. I do not think that the cutaneous lesions of this patient can all be due to a seborrheic dermatitis.

DR. J. L. GRUND, Boston: This case appears to be one of erythema multiforme bullosum. The patient states that she has had recurrent attacks of her present disorder, that they have been of short duration and that they have been accom-

panied by severe itching. She never had any fever, and her general health has always been normal. She has never had any lesions in the mouth. There is no evidence of scar tissue on the inner conjunctival surfaces of the eyelids. She presents a number of areas of erythema interspersed with flaccid bullae. The history and cutaneous appearance are not consistent with the picture of pemphigus.

DR. ARTHUR M. GREENWOOD, Boston: I have seen a case similar to this which fits into the so-called Senear-Usher syndrome, if there is such an entity. My patient has had bullae in the mouth and no involvement of the conjunctiva. Two Pels-Macht tests were negative. The Ashton-Welsh test was done once and did not show evidence of pemphigus. The patient is slowly getting better under treatment with small doses of gold and sodium thiosulphate intravenously. She has had several bad teeth extracted. The eruption presented is similar to that shown by my patient.

DR. BERNARD APPEL, Boston: The patient presented has had, in the past, definite small vesicular lesions on the conjunctiva.

DR. JOSEPH MULLER, Worcester, Mass: The diagnosis of pemphigus is favored by some members. I did not examine the patient thoroughly enough to make a diagnosis. At the Mayo Clinic a great deal of work on blood reaction has been done. I wish to call the members' attention again to the medicament used in Germany, namely, germanin, with which good results have been obtained. There have been some bad results, but not enough to contraindicate the use of the product in a case of pemphigus. I think the proper thing to do would be to try this product.

DR. J. L. GRUND, Boston: The product which Dr. Muller mentions is germanin, a German product, which before being used in the treatment of pemphigus, was employed successfully in the treatment of trypanosomiasis. Veiel first used it in four cases of pemphigus and reported good results. He believed that it would be of value against that condition because of the resemblance of some aspects (chronicity, fever and recurrence) of the disease to trypanosomiasis. The latest reports indicate, however, that the drug is valueless in the treatment of pemphigus. Zoon treated seven patients who did well with germanin; in two of them there was a recurrence of the disease followed by death. Bode reported on four patients, in all of whom the disease was aggravated during treatment. The lesions persisted under further treatment with germanin.

DR. JOHN G. DOWNING, Boston: As soon as I looked at this patient I agreed with Dr. Blaisdell's diagnosis. I saw definite bullae arising from the clear skin. There is no question of the possibility that the condition is of the Senear-Usher type. Clinically it has proceeded along the course of pemphigus. The contents of the bullae have been examined, and no streptococci were found. Also the blood has been sent to Dr. Pels, but no report has been received as yet. Regarding the use of germanin, I talked with a physician in New York who stated he had had disastrous effects from its use.

A CASE FOR DIAGNOSIS. Presented by DR. BERNARD APPEL, Boston.

This woman, aged 21, states that one year ago brownish, slightly itchy spots appeared on the back of the neck. They became slowly and progressively worse and spread down the back and then involved the upper part of both breasts and finally the middle portion of the abdomen. The lesions started as pink areas which ultimately became pigmented. At first they were itchy, especially at night; recently there has been no itching.

There are smooth, pigmented, macular areas in a mosaic pattern over the back of the neck, on the upper part of the breasts, at the midline of the abdomen near the umbilicus and in the center of the lower portion of the back. The areas are made up of macules about 0.5 to 1 cm. in diameter. Several areas have a shiny lichenoid appearance. There is no scarring and no marked atrophy. The lesions are symmetrical.

The Kahn reaction of the blood was negative. The examination of the urine gave normal results.

The patient has received treatment with salicylic acid and sulphur ointment.

DISCUSSION

DR. WALTER T. GARFIELD, Boston: I suggest the diagnosis of dermatitis herpetiformis.

DR. JOSEPH MULLER, Worcester, Mass.: There are a few lesions which look like round, slightly elevated papules. The patient states that the eruption started with the appearance of such lesions. The present condition is an after-effect, i. e., pigmentation, of some papular rash which is no longer clearly discernible.

DR. HARRY BAILEY, Hartford, Conn.: This case reminds me of one I observed recently in New York at the Academy of Medicine. There is pigmentation with areas of depigmentation. I suggest the diagnosis of achromia parasitica.

DR. WALTER T. GARFIELD, Boston: In justification of my diagnosis, I wish to say that these lesions seem symmetrical and grouped and that the pigmentation has persisted. Eruptions of dermatitis herpetiformis do not necessarily need to be vesicular. The patient has healed lesions.

DR. MAURICE J. STRAUSS, New Haven, Conn.: I wonder whether the areas of depigmentation to which Dr. Bailey refers do not appear as depigmentation merely through contrast with the hyperpigmented area. I could not detect any depigmentation.

DR. ARTHUR M. GREENWOOD, Boston: I think there is a possibility of spreading, superficial nevi. I admit that such a condition would be extremely rare.

DR. E. LAWRENCE OLIVER, Boston: It seems to me that what the patient presents is the terminal stage of a condition. I do not see how a diagnosis can be made. One can suspect various diseases, but I do not see how one can prove anything. The pigmentation may be due to many causes, i. e., dermatitis herpetiformis, lichen planus, etc. The perfumes the patient uses may cause this type of pigmentation.

LUPUS ERYTHEMATOSUS OF THE LOWER LIP. Presented by DR. WILLIAM J. MACDONALD, Boston.

This woman, aged 21, was presented at a meeting of the society in 1932, at which time she was suffering from lupus erythematosus of the eyelids and adjoining frontal area. The eruption followed exposure to sunlight and disappeared under treatment with gold sodium thiosulphate. The present eruption appeared without any obvious cause. The cosmetics the patient used were apparently not a causative factor; there is no history of self-medication.

The lower lip shows small cracks and slight bleeding; the lesions are painful.

The Wassermann reaction was negative.

No treatment has been given.

DISCUSSION

DR. WILLIAM J. MACDONALD, Boston: This patient was presented before the society a year ago with lesions on the upper eyelids which were diagnosed by all the members as lupus erythematosus. She had received gold sodium thiosulphate, and the lesions cleared up rapidly. Before that she had a tuberculous gland in the neck. The lesion on the lower lip is the only one present now. It is not due to any particular external application. The patient is presented as having lupus erythematosus. Treatment with gold and sodium thiosulphate will be started at once.

DR. E. MYLES STANDISH, Hartford, Conn.: I noticed a superficial silvery scaly lesion behind the right ear. I wonder whether or not a differential diagnosis between psoriasis and lupus erythematosus should be made.

KERATODERMA BLENNORRHAGICUM (?). Presented by DR. JOHN G. DOWNING, Boston.

This man, a chauffeur aged 29, has had a discharge from the urethra for three months before entrance to the hospital. Three weeks ago an eruption was first noted on the feet. One week later the eruption spread to the legs, body and arms; coincidentally with the spreading of the eruption swelling and a thermal reaction appeared in both ankles. Ten days later both knees swelled and began to ache. Before he sustained a sprain of the ankle, five weeks before entrance to the hospital, the patient had been taking capsules of sandalwood and instilling mild silver protein in the urethra twice a day for five weeks. No other medication except application of alcohol and mercury ointment to the cutaneous lesions on the feet has been given.

On both soles are large areas involving almost the entire plantar surface. There is a rather sharp line of demarcation, the lesions consisting of raised edges of dead skin with reddish-brown central areas of sloughing skin. A small replica of the large lesions appears between the toes and about the ankles. In addition there are firm, rounded, red, raised papules which look as though they might be deep vesicles but on palpation are found to be hard and keratotic. In the groin to the left of the scrotum there is an area approximately 3 by 2 cm. of somewhat similar reddish-brown central tissue with a hard border of brawny skin. In addition to this there are single lesions of similar nature from 3 to 15 mm. in diameter scattered rather thickly over the hips and sparsely over the back, chest and abdomen, and there are a few lesions over the arms, not exclusively located on either extensor or bolar aspects. Apparently the position of choice is to a certain extent on the points of irritation; however, on one knee and on an elbow there are rather small lesions, and lesions are present on the bolar aspects as well. The central portions of these lesions are firm and cannot be removed.

The Kahn test was negative. A complement-fixation test for gonococci was positive on Sept. 29, 1934. The examination of the urine gave essentially negative results. On Sept. 29, 1934, the right knee was tapped and 110 cc. of thick yellow fluid removed. Examination of this fluid showed 35,300 white cells, 96 per cent polymorphonuclears, 2 per cent lymphocytes, 1 per cent mononuclears, and 1 per cent clasmatocytes. A tapping of the left knee yielded 115 cc. of thick yellow fluid. On examination this fluid was found to contain 23,400 white cells, 91 per cent polymorphonuclears, 2 per cent lymphocytes, 1 per cent mononuclears and 6 per cent clasmatocytes. A complement-fixation test was positive for gonococci. A smear of material from the urethra was positive for gram-negative diplococci. Culture of the blood showed diphtheroid bacilli. On Oct. 31, 1934, culture of material from a cutaneous lesion showed Staphylococcus aureus and Staphylococcus albus but was negative for gonococci.

Hydrous wool fat, U. S. P., was applied to the affected areas, and the patient received autogenous gonococcus vaccine at first subcutaneously and later intravenously.

DISCUSSION

DR. J. L. GRUND, Boston: There are no lesions characteristic of keratoderma blennorrhagicum. There are, however, on the elbows and on the adjacent portions of the arms infiltrated erythematous plaques with superimposed dry silvery scaling. On the skin of the middle and lower portions of the back are large, raised, sharply defined and infiltrated plaques, each one of which contains a number of areas of dried papillary bleeding. The lesions are typical of psoriasis and do not at all resemble the nodular and horny lesions usually associated with keratoderma blennorrhagicum. There are certainly no lesions of the latter type on the palms and soles; the soles present a number of small areas of slight hyperkeratosis, and the palms show the remains of lesions which could well have been originally psoriatic. The entire cutaneous picture is that of psoriasis.

DR. VINCENT RYAN, Providence, R. I.: I looked at some of the photographs presented. They show evidence suggestive of keratoderma blennorrhagicum, but I believe that the lesions on the back are typical psoriatic lesions.

DR. EDWARD W. KARCHER, Lynn, Mass.: In view of the psoriatic lesions presented by this patient, it is interesting to note that Pusey in his book refers to Adamson's suggestion that keratoderma blennorrhagicum is a manifestation of psoriasis.

DR. C. GUY LANE, Boston: I think that one of the most striking features is in the nails. The small semicircular, sharply outlined, yellowish-brown areas toward the distal borders of the nails are suggestive of psoriasis. This feature together with the other lesions on the body indicates that the patient has psoriasis now, at least.

DR. JOHN G. DOWNING, Boston: This case further revives the time-honored discussion of a diagnosis of psoriasis or gonorrheal keratosis. Adamson contended that all cases showing the symptoms exhibited by this patient were cases of psoriasis. In psoriasis this triad of symptoms—urethritis, arthritis (positive complement-fixation test) and lesions on the palms and soles—is not present, and then again in gonorrheal keratosis the recurrence of attacks which occurs in psoriasis does not appear. This is the third case discussed here. In the other two cases the lesions and the arthritis cleared up after vesiculectomy. In this last case permission for vesiculectomy was refused. The patient still has lesions on the palms and soles. The lesions on the elbows are fairly typical of psoriasis. With regard to the lesions on the palms and soles, one cannot discard the diagnosis of keratoderma blennorrhagicum.

DR. BERNARD APPEL, Boston: I saw this man in consultation in the medical service about two and one-half months ago. I did not remember him today because the clinical picture he presents has changed so much. The patches on the body which now so closely simulate psoriasis were much more infiltrated and not so scaly. The lesions on the palms and soles presented the classic picture of what is generally accepted as being keratoderma blennorrhagicum. Now he shows lesions which, I believe, are typical residual lesions of keratoderma blennorrhagicum because they are deep-seated, small and definitely circumscribed and do not resemble the more flat and superficial type of keratosis which is usually seen in cases of psoriasis of the palms and soles.

DR. VINCENT RYAN, Providence, R. I.: I suggest that a biopsy be made from the psoriasis-like lesion on the back. After looking at some photographs of this man's feet taken several weeks ago, one could accept the diagnosis of keratoderma blennorrhagicum of the feet. However, the eruption on the body is typical of psoriatic lesions, and they keep appearing in spite of the treatment.

PSORIASIFORM SYPHILID. Presented by DR. HENRY BENJAMIN, Medford, Mass.

This man, aged 35, has had scaly erythematous patches on the extensor surfaces of the elbows for one year. No other lesions were present until three months ago. At that time he had a "severe cold" and a "bad sore throat." He took eleven boxes of acetylsalicylic acid tablets, some quinine pills and some other pills—all within two weeks. One week later a generalized rash appeared.

There is a diffuse pharyngitis. On the left tonsil there is a deep punched-out ulceration. A mucous patch is present on the inside of the left part of the lower lip. The body shows a generalized eruption consisting of infiltrated brownish-red macular lesions of various sizes and shapes, ranging from lesions 3 inches (7.6 cm.) long on the extensor surfaces of the elbows to small nodular ones on the chest and face. Most of the lesions are scaly, but some have hemorrhagic crusts in the center. There is generalized adenopathy. The foreskin is thickened and cannot be retracted. A thin serous discharge is visible underneath it.

The Kahn test, made on December 4, was positive.

The patient has received yellow mercurous iodide, ¼ grain (0.016 Gm.) three times a day, and two injections of bismuth subsalicylate.

DISCUSSION

DR. VINCENT RYAN, Providence, R. I.: I think that this patient presents two distinct types of cutaneous lesions: On the face he has lesions of a secondary

syphilis. When he was questioned he stated that these lesions were disappearing faster than those on the body. The generalized eruption impressed me as being definitely psoriatic. I have never seen an eruption of psoriatic syphilis as generalized as the one shown by this patient.

Dr. Austin W. Cheever, Boston: As I got the story, the patient had lesions on the elbows long before he acquired syphilis. Some of the lesions are improving under treatment. The lesions on the elbows impress me as being those of pure psoriasis. Two or three lesions around the trunk impress me as lesions of pure syphilis. I think that the greater part of the eruption is composed of a combination of psoriatic and syphilitic lesions. I believe that if antisyphilitic treatment is given the lesions on the elbow will persist.

Dr. J. Harper Blaisdell, Boston: I agree with the multiple diagnoses offered. The patient gave me the same facts and stated that a new type of eruption had appeared in the last three months, i. e., the lesions about the face and nose, which to my mind are good examples of syphilitic papules. In my opinion the eruption is more or less a dual condition. As to how long syphilis has been present, that is an interesting point. There has been no exposure in recent years. The Wassermann and the Kahn test of the blood of the patient's wife and child were negative. I believe that the syphilitic process has existed for a considerable period.

Dr. William P. Boardman, Boston: A Negro woman with similar lesions recurring several times was presented at a meeting of the society about a year ago. Each exacerbation cleared up under treatment with potassium iodide alone or in combination with arsphenamine. That treatment cleared up some lesions of psoriasis, but it was evident that the patient's condition did not improve until she received antisyphilitic treatment. However, the last time she was seen the antisyphilitic treatment did not clear up the condition. I think the disease finally turned out to be mostly psoriasis. I saw a physician with a similar recurring eruption localized around the scrotum and genitalia. He had definite evidence of psoriasis long before he acquired syphilis. I could not tell which was which. Sometimes potassium iodide cleared up the condition and at other times chrysarobin did so, but in this case it is not known how long the patient has had syphilis. The results of treatment are not conclusive. Arsphenamine may clear up the eruption at the elbows, if the condition there is psoriasis, but psoriatic syphilids appear definitely on the elbows, and when such lesions finally clear up they never recur.

Dr. Myer M. Tolman, Chelsea, Mass.: The patient also has numerous punched-out ulcers on the genitalia. I think that can be regarded as a late recurrence of secondary syphilis.

Dr. William J. MacDonald, Boston: Have the members used di-hydroxyanthranol? I have used it in several cases of psoriasis with good results. Possibly its use in this case would cause the lesions to disappear.

Dr. Rudolph Jacoby, Boston: I do not think it would be extraordinary if the lesions cleared up under antisyphilitic treatment. The consensus seems to be that the patient has two different conditions, i. e., syphilis and psoriasis.

Dr. Henry Benjamin, Medford, Mass: Although the lesions on the elbows have been present for a year, the other lesions on the body seem to have appeared about three months ago. In my opinion that indicates that all the lesions that appeared suddenly at the time the second outbreak occurred should be considered lesions of secondary syphilis.

Keratosis Palmaris et Plantaris (Arsenical). Presented by Dr. Ellwood C. Weise, Bridgeport, Conn.

This patient was presented at a meeting of the society on Oct. 10, 1934 (Arch. Dermat. & Syph. **31**:574 [April] 1935).

DISCUSSION

Dr. E. Myles Standish: Dr. Weise informed me that an examination of the urine showed arsenic to be present in abnormally high amounts.

## PHILADELPHIA DERMATOLOGICAL SOCIETY

VAUGHN C. GARNER, M.D., *Secretary*

*Dec. 13, 1934*

ROBERT L. GILMAN, M.D., *Chairman*

ACNITIS. Presented by DR. EDWARD F. CORSON.

This man, aged 29, had furunculosis at 12 years; moderate hemoptysis has occurred in the past three years. He had a gonorrheal infection three years ago, which was treated for seven months and followed by epididymitis on the right side. He states that he did not have a primary lesion. He has not indulged in the use of alcohol since the facial eruption began. One year ago small papulopustular lesions appeared on the face, and six weeks later the condition became manifest on the penis. The urinalysis and the blood count gave normal results.

DISCUSSION

DR. E. D. WEIDMAN: Over the shoulders, on the shaft of the penis and in a few other places there are some deep-seated, yellowish nodules over which the skin is freely movable. The lesions on the face are not of that character, and I do not know whether the two conditions are related. I tried to obtain a history, but the patient is not a medical observer. The lesions on the face are erythematous; they rupture and ooze, and it is theoretically possible that they are of the same type as the ones on other parts of the body, but have ruptured and become secondarily infected. However, I do not think that is the case. It would be instructive to make a biopsy on those two different types of lesions to determine whether the lesions on the face were cystic reactions of the sudoriparous apparatus and the yellow ones on other parts of the body, cystic reactions of the sebaceous apparatus. All the members will recall the cases of steatocystoma multiplex which Finnerud has described, and I vaguely recall seeing a patient who had lesions of a more translucent appearance. I wondered whether there was also involvement of the sweat glands, but of course I could not discuss that question because it would not have led anywhere without a biopsy. Now these lesions are regarded as congenital anomalies. According to the well known principle of general pathology that when there is an anomaly of one part of the body there is likely to be an anomaly of some other part, I think that, particularly in view of the fact that the sebaceous and the sudoriparous apparatus have a common embryologic origin in the skin plate of Remak, one could expect to find combinations of steatocystoma and syringocystoma multiplex. This is an interesting case; biopsies on these two types of lesions might throw much light on it. I doubt that the condition is a tuberculid. I might concede that it is acnitis, but I do not think that it is tuberculous. One ought not to consider the case closed until a microscopic examination of the lesions has been made.

DR. S. S. GREENBAUM: I agree with Dr. Weidman that it would be interesting to compare the histologic picture of the lesion on the penis and that of the one on the face, but my impression is that clinically the lesions on the face, at least, will turn out to be definitely tuberculous. But I do not believe that they belong in the acnitis group.

ROENTGEN DERMATITIS. Presented by DR. H. G. MUNSON for DR. FRANK C. KNOWLES.

This man, aged 29, says that ten days after an extensive fluoroscopic examination for a piece of steel in the right index finger made in March 1934, there developed a dermatitis followed by successive desquamations of the skin of the right hand. The affected part was treated with trinitrophenol. The patient complained of decreased sensation, slight numbness and some loss of power in the right index finger. Redness and thinning of the skin of the affected region were noticeable.

DISCUSSION

DR. C. P. WRIGHT: Perhaps some of the members know the notoriety given to the work of Dr. Collins in the treatment of burns due to roentgen rays with the plant Aloe vera. This is a novel method of treatment. I have not tried it on a burn due to roentgen rays, but in one or two cases of sluggish conditions, particularly in a case of ulcer of the leg, healing was rapid. The fresh plant itself is applied directly to the wound, and in twenty-four hours all the gummy, resinous substance within the plant penetrates into the skin; the patients are surprised at the way the skin seems to absorb this substance from the plant. Dr. Collins is enthusiastic about the use of the plant in burns due to roentgen rays. His work was reported, I believe, before the American Roentgenological Society. The difficulty is that one has to send to Florida for the plants.

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA OF HABERMAN. Presented by DR. HERMAN BEERMAN.

This well nourished boy, aged 11 years, presented an eruption of about four months' duration. It began insidiously, was not preceded by any particular indisposition and was not associated with pruritus. On Nov. 10, 1934, there appeared on the trunk and proximal segments of the extremities an eruption consisting of the following types of lesions: (1) yellowish infiltrated papules, some associated with small areas of telangiectasis, (2) papules surmounted by a small vesicle, (3) excoriated papules and (4) atrophic macules. The lesions show a tendency to be distributed along the line of cleavage. There are no lesions on the palms and soles and no lesions of the mucous membrane. There are no lesions in the genital region. At first glance the general appearance of the eruption suggests varicella. At present there is some involution of the entire process, and the eruption is concentrated especially on the anterior aspect of the trunk. There is no abnormality of any of the internal organs and no adenopathy. Serologic tests of the blood were negative. A search for fungi and molluscum organisms gave negative results. Biopsy on an early lesion from the left flank showed a slight amount of keratotic material on the surface with the granular layer reduced to a single layer. At one spot there was a fragment of parakeratotic material. The epidermis was thickened and highly edematous, and in places the appearance was suggestive of beginning microscopic vesicles. The basal layer was disorganized, merging with the cutis. The papillae were edematous, and there was a round cell infiltration in the corium. There were no hairs in the sections, and except for a slight hyperkeratosis at the mouth of the ducts the sweat apparatus was normal. Treatment with 2.5 per cent ointment of ammoniated mercury and ultraviolet radiation produced a slight involution in six weeks.

DISCUSSION

DR. F. D. WEIDMAN: I think there is something distinctive about the lesions of the patient whom I presented this evening. Of course the diagnosis of Haberman's disease is based on the scars, the scale and the early appearance of the vesicles. I think, too, that the primary lesion is rather distinctive. It differs from the vesicle of eczema. If one runs a finger over it, it is shotlike and feels somewhat like a lesion of chickenpox. It promptly dries up into a gummy crust which can be picked out. Although in Dr. Beerman's patient the condition is not fully developed, there are a few lesions left to pass on, and I must confess that I am influenced by the character of the primary lesion to support his diagnosis.

DR. HERMAN BEERMAN: It is somewhat more difficult to make the diagnosis now than it was originally. Since I first observed them the lesions have regressed considerably; the histologic structure of the earliest lesion bore out the diagnosis of Haberman's disease. I do not know of any vesicles ever having occurred in cases of pityriasis lichenoides chronica.

DR. ABRAM STRAUSS: There are several lichenoid lesions on this boy's arm. I was inclined to believe that this might be an eruption due to a drug or lichen urticatus.

DR. HERMAN BEERMAN: The lesions on the legs resemble eczematoid dermatitis, but the case impressed me at first as being one of Haberman's disease.

DR. FRANK C. KNOWLES: I think dermatologists are seeing a large number of cases of an extremely rare disease. It may be that since attention has been called to that condition they are more critical of this diagnosis. I should have regarded this case as one of papulonecrotic tuberculid. The lesions are located on the nose, and there are pitlike scars on the body; also, there are scaly places that one would hardly notice unless one observed the patient closely. The hard, pitlike lesions suggest a papulonecrotic tuberculid of unusual distribution, although there is a scar on the nose, which is more typical of Haberman's disease. It is wise to try to find these rare conditions, but it seems rather curious that so many of these cases should be suddenly discovered in one city.

DR. J. V. KLAUDER: I think the patient has erythema multiforme.

LICHEN PLANUS COMPLICATED BY INVOLVEMENT OF THE NAILS; PITYRIASIS ROSEA COINCIDENT WITH LICHEN PLANUS. Presented by DR. HERMAN BEERMAN.

This man, aged 31, presents an eruption on the trunk and extremities. The condition appeared on the arms in February 1934. There was slight pruritus, but no general indisposition was noted. The condition was not associated with unusual pressure. Examination revealed typical lichen planus with lesions in the usual distribution at points of pressure. Some of the lesions were annular, and some occupied marks of scratching. The patient was given one dose of roentgen radiation and other local treatment in April 1934; after that he was not seen until September. Two months before that visit the nails of the fingers suddenly began to wear away from the lunula, and the condition progressed to the point of lifting practically all the nails of the fingers and those of both big toes. The general health had been good. Except for a few residual lesions the eruption had disappeared. The nail beds were exposed to roentgen radiation, soaked in potassium permanganate and treated with a modified Whitfield's ointment. Early in November 1934 it was noted that on the left forearm and right shin and in scattered situations typical lesions of lichen planus had reappeared. On November 21 examination revealed in addition to the lichen planus a typical pityriasis rosea somewhat urticarial in character but with intermingled medallion lesions. At that time pruritus of notable intensity was present for the first time. On November 28 an annular lesion of lichen planus appeared on the penis. By December 5 the pityriasis rosea as well as the pruritus was practically gone. During all that time the status of the nails remained about the same.

The patient is obese and healthy-looking. There are traces of lichen planus on the extremities, an annular lesion on the penis and questionable mucosal lesions. The nails of all the fingers of both hands are practically destroyed. The remnants are somewhat discolored and grooved by longitudinal fissures and flutings, and the entire nail plate is raised from the nail bed, which is erythematous and somewhat swollen. The nail of the middle finger of the left hand is least affected, although the earliest changes, brittleness, discoloration and slight ridging, are beginning to appear. The nails of both big toes are thickened and yellow, and the underlying bed is covered with débris. There are no gross abnormalities, no adenopathy and no involvement of peripheral nerves. Serologic tests of the blood were negative. The scrapings from the finger-nails and toe-nails were negative for fungi. No biopsy has been made. The patient has received roentgen radiation, yellow mercurous oxide and whole blood; he has also been treated with local application of ointments and starch baths.

DISCUSSION

DR. J. V. KLAUDER: I have never seen a patient with lichen planus of the nails, although some cases have been reported.

DR. S. S. GREENBAUM: Several cases of lichen planus with changes in the nails have been described. I have seen a patient with just this type, in which there has been three or four sheddings of all the nails of the hands and feet. The agent that causes lichen planus seems to have some effect on the secretory mechanism of the nail matrices, although in my case there was, I think, a definite papule of lichen planus on one of the nail beds.

DR. FRANK C. KNOWLES: I believe that this is a case of tinea of the nails coincidental with lichen planus. A friable condition of the nails speaks strongly for the diagnosis of fungous infection. All the members know that it is probably more difficult to obtain fungi from nails than from lesions on any other part of the body. Fungus is sparse in many cases, and several examinations may have to be made before a positive result of examination is obtained.

DR. ABRAM STRAUSS: I am rather inclined to agree with Dr. Knowles because one sees so many cases of lichen planus with no involvement of the nails and a great many cases of involvement of the nails without lichen planus; this makes me believe that the occurrence of the two conditions in one patient is rather a coincidence.

DR. S. S. GREENBAUM: Were the nails scraped and scrapings cultured?

DR. HERMAN BEERMAN: This case is apparently full of coincidences: There developed a typical pityriasis rosea which caused pruritus; this had not been present before and has not occurred since. The nails of all the fingers and some of those of the toes have been studied for fungi on many occasions with negative results.

A CASE FOR DIAGNOSIS. Presented by DR. R. E. IMHOF.

This woman, aged 33, the mother of three children, presents on the right upper extremity a mottled erythema with several atrophic scars in the region of the elbow. The condition is of one year's duration. There are livid discoloration of the right upper extremity, coldness of the fingers and, occasionally, dull pain. There have been no previous acute illnesses or operations. The reflexes and sensation for pain and touch are normal. The Wassermann test was negative. Roentgen examination revealed no cervical rib and no bony lesion in the right elbow.

DISCUSSION

DR. F. D. WIEDMAN: I cannot make a diagnosis at present. I do not think that the condition is early scleroderma; it has lasted too long to be still in the infiltrative stage. I wonder whether it is a kind of dermatomyositis. The patient says she has had pain, and while there is no history of rheumatism I think the possibility of rheumatism could be considered in this case. A leukocyte count and a biopsy would be helpful; the histologic picture of rheumatism of the skin is rather distinctive. I should make a tentative diagnosis of a rheumatic condition in the skin, possibly dermatomyositis.

DR. S. S. GREENBAUM: The patient presents, particularly over the right arm, a variable number of atrophic macules the size of a split pea and larger. Whether these macules are a part of the erythematous picture or not I do not know. I suggest the diagnosis of an early stage of acrodermatitis chronica atrophicans or of scleroderma.

DR. F. D. WEIDMAN: Some cases like this one in which pain and edema are present have been found to be cases of trichiniasis. While few cases of trichiniasis are seen in this part of the country, the possibility should not be forgotten. Eosinophilia is the first diagnostic sign.

A CASE FOR DIAGNOSIS. Presented by DR. ROBERT L. GILMAN.

This man, aged 21, presents an annular and linear pruritic lichenified patch of fourteen months' duration; the eruption extends from the midline of the neck to within the hair line on the right side. No laboratory studies have been made. Biopsy showed mild acanthosis around the hair follicles and perivascular leukocytic infiltration and fibrous tissue about other vessels. Di-hydroxy-anthranol 0.25 per cent has been used with fair results.

DISCUSSION

DR. FRANK C. KNOWLES: I think it is naevus unilateralis comedonicus. Some of the follicles seem to be dilated, and some, obstructed. There is a slight sug-

gestion of comedo formation. From the appearance the eruption is rather typical of that condition.

DR. ROBERT L. GILMAN: The results of biopsy do not suggest that diagnosis, but the specimen was taken too low down. The boy states that the condition has been present for only fourteen months.

DR. FRANK C. KNOWLES: This is the acquired type, and there may be further development.

DR. F. D. WEIDMAN: I wonder whether there is a factitious element.

DR. ROBERT L. GILMAN: That appearance may be due to the ointment the patient has been using.

DR. ABRAM STRAUSS: Has any roentgen therapy been applied?

DR. ROBERT L. GILMAN: No, there has been no such therapy.

HIRSUTIES. Presented by DR. J. M. SCHILDKRAUT, Trenton, N. J.

This girl, aged 5 years, presents a marked overgrowth of hair over the entire body; the hair is long and heavy over the arms, back and legs; it is short and black on the face. The characteristics, aside from the growth of hair, are female. She is presented for suggestions as to treatment.

DISCUSSION

DR. F. D. WEIDMAN: I think there should be more question of study than of treatment. There must be a glandular basis, such as pituitary or adrenal disturbance in this case. In the cases of adrenal disturbance there is hypertrophy of the cortex, resulting in extreme virilism; the cases of pituitary disturbance are associated with obesity and harshness and dryness of the skin. This patient does not have such additional stigmas of pituitary disease; therefore I think that she should be observed for adrenal disturbance.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: My co-workers and I considered the possibility of adrenal disturbance. There is a possibility of an ovotestis, but I thought that some of the members who have greater experience with glandular conditions might be able to give us some suggestions.

DR. S. S. GREENBAUM: I suggest refraining from treatment for the present.

PREMYCOTIC STAGE OF MYCOSIS FUNGOIDES. Presented by DR. EDWARD F. CORSON for DR. FRANK C. KNOWLES.

This woman, aged 47, presents large, sharply defined, rounded, pigmented superficial macules with scanty scaling. The scaling is a recent feature and is best seen on the arms, legs and buttocks. The patient has not used phenolphthalein for two years. Scrapings were negative for fungi. A blood count made recently gave normal results. The Wassermann and Kahn tests and the urinalysis gave negative results. Roentgen treatment has twice cleared the condition, but relapses occurred after months of normalcy. There was a doubt at first as to the influence exerted by phenolphthalein. This doubt was apparently dispelled by long observation.

DISCUSSION

DR. EDWARD F. CORSON: This patient was shown about a year and a half ago, and I recall that the members were rather undecided as to whether the condition was really mycotic or whether ingestion of phenolphthalein had changed the lesions to some extent. The patient is shown tonight merely in order to clear up that difficulty.

ERUPTION DUE TO PHENOLPHTHALEIN? DERMATITIS HERPETIFORMIS? Presented by DR. F. D. WEIDMAN.

This man, aged 31, shows slight pitting and deformation of the nails and slight hyperkeratosis of the palms and soles. When he was first seen there were

crusts on the scalp, on the backs of the hands and on isolated regions of the trunk. The condition was diagnosed as secondary dermatitis due to supermedication. The glans penis was red and tender. There was an erythematosquamous eruption on the face, trunk and extensor surfaces of the forearms and arms. He had used phenolphthalein up to one year ago, but since that time he had used only magnesium sulphate as a laxative. At present only slight erythema remains over the site of lesions on the cheeks. The crusts have disappeared from the scalp and other regions, but numerous excoriations remain on the legs and trunk. There are infiltrated, erythematous and slightly pigmented macules over the back of the chest, the backs of the hands and the abdomen, but these macules are disappearing. The glans penis is still diffusely red. In substance, the patient has an itchy eruption of the type of erythema perstans. The blood count showed: white cells, 15,900; eosinophils, 42 per cent; lymphocytes, 20 per cent, and polymorphonuclears, 38 per cent. The Kahn reaction was negative. The sugar and urea content of the blood were normal. The feces were negative for parasites and for blood. The patient was treated with starch baths and applications of antiseptic and antipruritic ointments.

DISCUSSION

DR. F. D. WEIDMAN: I should value the opinions of the members. So far as can be ascertained the patient has not taken any phenolphthalein for a year.

DR. HERMAN BEERMAN: Some time ago I showed a patient who had an eruption undoubtedly due to phenolphthalein. He had been warned about the drug, and he thought he had avoided taking it; but he told me that on two occasions after he had been intoxicated there developed an eruption similar to the eruption due to phenolphthalein. Apparently, therefore, the sites of previous eruptions due to phenolphthalein may show a flare-up due to causes other than the drug itself.

DR. F. D. WEIDMAN: Patients may ingest phenolphthalein without realizing it, for instance, by eating cakes with icing colored pink by means of phenolphthalein. I went into such considerations as exhaustively as I could with this patient. I think there is a possibility in what Dr. Beerman said.

DR. FRANK C. KNOWLES: It seems to me this eruption may be the remains of a fixed eruption due to phenolphthalein.

DR. ROBERT L. GILMAN: I do not believe that this patient's condition falls into the category of dermatitis due to scratching.

HABERMAN'S COMPLEX (DERMATITIS HERPETIFORMIS?). Presented by DR. F. D. WEIDMAN.

This girl, aged 12 years, has a papular eruption which began one year ago on the left leg. The lesions coalesced; then the other leg became similarly affected, and subsequently lesions developed on the hand. There was moderate itching. During August the lesions cleared up completely. At present the patient's general condition is good. She presents (1) deep-seated, shotlike, more or less grouped papules and vesicles located mostly on the knees, on the front of the legs and on the elbows, and isolated lesions on the arms; (2) numerous closely placed scars of uniform size (corresponding to that of the papules and vesicles) on the extensor surfaces of the arms and forearms and a small patch over the manubrium; (3) a fine, branny scale over the forearms and thighs. The face and neck, as well as the scalp, are free from lesions. There is no pigmentation. A provocative test with potassium iodide and a tuberculin test were negative. The urinalysis gave normal results. No biopsy has been made. Treatment with soothing ointments did not influence the course of the malady.

DISCUSSION

DR. ABRAM STRAUSS: This patient has many papular lesions and many areas of discoloration on the upper arm, remnants of previous attacks; this leads me to think that possibly she has lichen urticatus.

EARLY STAGE OF PRIMARY EPIDERMOID CARCINOMA. Presented by DR. S. KATZ for DR. S. S. GREENBAUM.

This man, aged 71, exhibited in September a quarter-sized ulcer of two weeks' duration, located on the anterior middle third of the right leg. He stated that itching had been present over the lower extremities for thirty years. The tissue surrounding the ulcer was the seat of a long-standing hypertrophic ulceration. The results of microscopic examination were reported as follows: Because of the definite epithelial downgrowth, the tendency to formation of whorls, the moderate polychromatism, the presence of isolated clumps of epithelial cells and the breaking through in some regions of the basement membrane, the case is regarded as one of an early stage of epidermoid carcinoma superimposed on hypertrophic lichen planus.

DISCUSSION

DR. J. V. KLAUDER: I agree with the diagnosis of malignant degeneration in a case of lichen planus hypertrophicus.

DR. C. S. WRIGHT: I agree with that diagnosis.

DR. ABRAM STRAUSS: I asked this patient about radiation therapy. He thought he had received roentgen therapy, and I believe that the condition may be attributed to the roentgen therapy in connection with the lichen planus.

DR. F. D. WEIDMAN: From the gross morphologic appearance I think that the condition is carcinoma, but from the appearance of the sections I do not think so. Of course, this is true only of the particular portion of the lesion taken for microscopic study. It may be that the entire lesion, if checked all the way through, would give a true picture of carcinoma. The sections submitted do not substantiate the diagnosis of cancer. However, I agree that the clinical manifestations resemble those of cancer.

DR. S. S. GREENBAUM: A pathologist definitely made the diagnosis of epidermoid cancer. My impression was that the case may be one of pseudo-epitheliomatous hyperplasia such as those reported by Dr. Weidman and Dr. White, but the clinical picture of the lesion seems to me to be that of epithelioma, and I think that the lesion should be treated as such.

SARCOMA CUTIS. Presented by DR. ABRAM STRAUSS.

This man, aged 55, says that in 1929 there developed on the left thigh a lesion about the size of an egg; this was excised, and a pathologic diagnosis of mycosis fungoides was made. The lesion then recurred, and about a year ago it was excised again; at that time another histologic diagnosis of mycosis fungoides was made. Massive doses of roentgen and radium radiation were given, and healing was followed by breaking down of the tissues which produced the present picture.

DISCUSSION

DR. C. S. WRIGHT: I saw a similar case about three or four years ago. Finally the woman's leg had to be amputated. The process extended in spite of every attempt at treatment.

DR. F. D. WEIDMAN: Since the patient was not completely disrobed, I did not have a chance to examine him as I should have liked to. However, it seemed that the involvement of the thighs was disproportionate to that of the parts below; this, I think, is rather contrary to the situation in granuloma fungoides. One would not expect a comparatively small, isolated cutaneous lesion of granuloma fungoides such as this patient exhibits to be accompanied by deeply infiltrated processes in the surrounding tissues. I think this points to sarcoma rather than to granuloma fungoides. On account of the intense radiation which had been applied the histologic sections did not yield information as to whether the condition is granuloma fungoides or one of the round cell sarcomas.

CIRCUMSCRIBED LEUKEMIA CUTIS. Presented by DR. J. M. SCHILDKRAUT, Trenton, N. J.

This man, a carpenter aged 45, presents a condition which began two years ago with inguinal adenopathy. At present all the lymph glands of the body are enlarged, especially those in the inguinal and axillary regions. Both nipples show a marked infiltration. On the back of the left hand there is a plaque of dusky red infiltration. There is a similar patch on the anterior surface of the left wrist. The tips of the second, third and fourth fingers of the left hand are thickened, infiltrated and dusky red. A fading patch is seen on the back of the right hand. Cutaneous manifestations have been present for the past four months. There is a history of similar lesions on the knees, which disappeared spontaneously. The spleen is definitely enlarged. A blood count made on Dec. 5, 1934, gave the following results: hemoglobin, 80 per cent; red cells, 4,420,000; white cells, 47,250; polymorphonuclears, 6 per cent, and lymphocytes, 94 per cent. On December 12 the blood count showed: hemoglobin, 70 per cent; red cells, 4,570,000; white cells, 72,800; polymorphonuclears, 3 per cent, and lymphocytes, 97 per cent.

DISCUSSION

DR. F. D. WEIDMAN: I think all the members agree that this is a spectacular case; there is no question about the diagnosis. The lesions on the hand are suggestive of leukemia cutis, even without the blood picture. If they had occurred around the face, that would have added more weight to the diagnosis. All the members are impressed with the similarity of the big plaques of infiltration to lesions of sarcoid and of Hansen's disease.

I was intrigued by the rosacea-like distribution on the face. One ought not simply to pause after making a diagnosis; one ought to try to figure out the nature of the general pathologic condition whereby such a peculiar distribution takes place in the skin. All the members are curious as to the cause of the butterfly distribution in lupus erythematosus and rosacea; now if the distribution of leukemia cutis is added to that of the aforementioned diseases, the question arises: What is there that is common to the three and determines that particular distribution? The members may recall that Dr. Jadassohn read a paper on the hematogenous dermatoses at one of the meetings of the American Dermatological Association. Personally I plan to refresh my memory as to his paper and to see whether there is a possibility that leukemic changes may in any way be reconciled with the anatomic peculiarities of the face. I do not think that this butterfly distribution is common. I should like to know about it.

DR. FRANK C. KNOWLES: I think this is one of the most unusual and interesting cases we have ever seen. A few cases of this description, in some of which there was a little more hemorrhage into the skin have been observed at dermatological meetings. In a case of this description it might be wise to try to determine the lead content of the body, and if the amount of lead in the system is decreasing, to consider giving the patient lead in addition to roentgen therapy over the long bones.

DR. J. V. KLAUDER: With particular reference to the color, I have never seen a leukemic infiltration of this character. I have never seen acne rosacea associated with leukemia. There is a question as to whether that is just a coincidence.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I am inclined to think that the patient has acne rosacea, but I feel that that, too, is part of the leukemia. There is a picture in Dr. Pusey's book which is almost a replica of this man's eruption; it shows the butterfly distribution and the infiltration on the backs of the hands and on the fingers.

TRICHORRHEXIS NODOSA. Presented by DR. THOMAS BUTTERWORTH.

This woman, aged 29, presents on the top of the head several places where the hair has broken off at about ¾ inch (1.9 cm.) from the scalp. The patient had dyed her hair for five years. For two months prior to the onset of the present

condition she used a double strength hydrogen dioxide bleaching agent. At about the middle of September, after the patient had a shampoo, large amounts of hair fell out. She had the hair trimmed to within ½ inch (1.27 cm.) from the scalp. When the hair grew again it broke off in four patches at a length of from ¾ to 1 inch (1.9 to 2.5 cm.). The Wassermann and Kahn tests were negative. Microscopically the hairs present ovoid brushlike nodes. Generally speaking, the nodes are scarce.

DISCUSSION

DR. THOMAS BUTTERWORTH: This is a fine example of what women will do. For five years the patient had red hair; then she decided that she wanted to be a blonde, and for two months she applied a double strength hydrogen dioxide bleaching agent. The hair came off at the scalp; then the patient stopped treatment for a while, and the hair began to grow again. In four or five places the hair had a wiry texture and did not grow as well as in the other places, so the patient went to a beauty parlor and began to submit to treatments with hot oil. The hair began to grow quite well on the side, but on the top of the scalp there was a sort of scrubby growth; under the microscope numerous nodes were seen on the hair. Three weeks ago all treatment was discontinued, and the patient was not even allowed to comb her hair. It is really embarrassing to see how well the condition has responded to the absence of all treatment.

DR. ABRAM STRAUSS: How is the patient's nervous system?

DR. THOMAS BUTTERWORTH: She is introspective.

DR. ABRAM STRAUSS: I believe if one could tie her hands she would get better quicker.

MULTIPLE HEREDITARY TELANGIECTASIA (RENDU-WEBER-OSLER SYNDROME). Presented by DR. DONALD M. PILLSBURY.

This well nourished man, aged 52, presents multiple small telangiectatic papules on the face, right conjunctiva, tongue, soft palate, scalp, shoulders and fingers. The heart is markedly enlarged, there are signs of probably rheumatic valvulitis and the liver and spleen are palpable. Roentgen examination of the skull showed a marked increase in the size of the venous tracts. The red blood cells numbered 3,000,000, and the hemoglobin was 42 per cent; the number of white blood cells and the results of the differential count were normal. The patient's blood is type 4. A biopsy has not been made. The patient states that telangiectatic spots have appeared for the last ten years. He has had repeated attacks of epistaxis and suffered from cardiac decompensation on one occasion. He states that his father had repeated attacks of epistaxis and died of hemorrhage during an attack. Two brothers and one son also had repeated attacks of epistaxis. The patient's mother and daughter are not affected.

DISCUSSION

DR. F. D. WEIDMAN: I think that all the members agree as to the diagnosis. I merely want to point out the rather significant distribution of many of the lesions. The patient showed the lesions at the tips of the fingers. I also noticed one under the nail of the little finger of the left hand, which strikingly recalls the distribution of the normal glomi of the skin. It is true that the lesions of this patient are not black, and are not venous but arterial, and that appears to militate against a connection with glomi as they are now known. The subject of arteriovenous anastomosis of the skin comes to the forefront, now that these subungual tumors have been referred to them. I wonder whether one effect of this hemorrhagic complex is not to bring to light anastomoses present elsewhere in the skin. It may be that this disease is signaling certain special anatomic locations of the body where there are some special anatomic structures which may be, like glomi, abnormal or at least special arrangements of the blood vascular system. I think it would be worth while to examine these lesions by a reconstruction technic and see whether there is something more than an ectasia of ordinarily normal capillaries.

DR. S. S. GREENBAUM: Are the lesions on the hands areas of telangiectasia or angiomas?

DR. HERMAN BEERMAN: They are telangiectatic.

DR. S. S. GREENBAUM: I recently saw a case of angiomatosis. Three persons in the same family had the disease, but the patient I saw had definite pinhead-sized and larger angiomas on the thumb. He also had some areas of telangiectasia on the skin and suffered from nasal telangiectatic lesions.

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## DETROIT DERMATOLOGICAL SOCIETY

WILLIAM G. SAUNDERS, M.D., *Secretary*

*Regular Meeting, Dec. 18, 1934*

CLYDE K. HASLEY, M.D., *President*

CYSTIC ACNE. Presented by DR. CLYDE K. HASLEY.

R. K., a schoolboy aged 14, has a severe type of acne of about one year's duration. He is presented to show the results of intravenous administration of 1 minim (0.06 cc.) of typhoid vaccine given about one week ago. No other treatment was used. Later after the patient has had more of this type of therapy he will be shown again. Marked improvement has followed the one treatment.

DISCUSSION

DR. CHESTER A. DOTY: I use the type of typhoid therapy that Dr. Hasley has been using, namely intravenous injection of 10,000,000 organisms in 10 cc. of saline solution. In a number of these cases of chronic acne, I have obtained the same result as Dr. Hasley has. The eruption usually reappears in about six months. Five injections are given at intervals of five days. The reaction is more severe if more than five days elapse between treatments.

DR. ARTHUR E. SCHILLER: My co-workers and I have found this method of treatment quite successful. I believe that a blood count should be made. If the count is low the results are far better than if it is high. On the average, the majority of patients with this type of acne have a low number of white blood cells.

DR. EMMETT C. TROXELL: Have the results of typhoid therapy been compared with those of intramuscular administration of foreign protein?

DR. ARTHUR E. SCHILLER: My co-workers and I used injections of milk and obtained rather poor results. We also used old tuberculin but the results were not good. We use 1 minim (0.06 cc.) of typhoid vaccine at first. The vaccine is diluted with 5 cc. of sterile distilled water. The second dose is 4 minims; the third, 5, and the fourth, 8 (0.24, 0.3 and 0.5 cc., respectively). Rather severe reactions have followed the fourth injection.

DR. JOHN A. HOOKEY: Dr. Doty says that these conditions clear up in about six months. I wonder whether better results would be obtained if the interval between courses of treatment was shortened.

DR. H. S. BARTHOLOMEW: I believe that the improvement and the length of time required for it to take place depend on the age of the patient.

DR. ARTHUR E. SCHILLER: In some of the cases the chill appears in forty-five minutes. It may last from thirty minutes to an hour and a half. The entire syndrome is over in about eight or nine hours after the chill.

DR. H. S. BARTHOLOMEW: I have seen the chill appear in ten minutes.

DR. G. WARREN HYDE: I wonder whether any one has tried treating cystic acne with preparations of bismuth such as thio-bismol given intramuscularly. Physicians in Chicago report excellent results obtained by this method, but they combine roentgen therapy with the administration of thio-bismol.

If the members have any more patients who are being treated with typhoid vaccine, I should like to hear reports of the results at future meetings, as good results obtained in this type of cases by any method are certainly gratifying and worth reporting.

A Case of Erythema Induratum (Tuberculosis Cutis). Presented by Dr. Harther L. Keim.

F. R., a German-American woman aged 25, a domestic worker says that during the past six months she has lost 20 pounds (9.1 Kg.) and has been unusually tired. The disease began in April 1934 with the appearance of the first lesion on the left thigh. This was slightly painful; it enlarged slowly and, after softening, broke down and discharged a hemorrhagic exudate. Since that time many lesions have appeared, particularly on the legs. After going through a cycle similar to that described for the first lesions the subsequent eruption finally healed.

At present the lesions are especially numerous on the lower extremities, but some are found on the forearms and abdomen as well. They are in various stages of evolution. Three types of active lesions are present:

1. Nodules arising in the hypoderm and varying in size from that of a large pea to that of a walnut. These nodules soften, break down and leave a discharging sinus; occasionally they are absorbed. 2. Smaller deep-seated nodules. These lesions undergo necrosis and terminate in a sharply punched-out ulcerative lesion. 3. Groups of superficially situated small dry brownish nodules which apparently do not break down. These are associated with slight desquamation.

The healed lesions appear as scars with a depressed and irregular outline. Pain is not a striking symptom. No biopsy specimen has been obtained.

Roentgen examination of the chest did not show evidence of tuberculosis. The tuberculin test was negative.

DISCUSSION

Dr. Loren W. Shaffer: I think this patient exhibits an unusual condition. I do not think that there is any question about the diagnosis of tuberculosis. The classification and type of the lesions are the one subject of argument. The patient is of rather blond type, and her age corresponds to that at which erythema induratum usually appears. The lesions on the thigh and those on the legs are typical of the nodules seen in erythema induratum. Personally, I think that too much effort is made to classify tuberculosis of the skin and to fit the symptoms in certain groups. In the light of the microscopic picture, I think that the diagnosis of tuberculosis of the skin with erythema induratum-like lesions would be more accurate.

Dr. Harther L. Keim: I made a definite diagnosis of erythema induratum especially to bring out the points to which Dr. Shaffer referred. This patient is a young woman; the lesions occur predominantly on the legs and are for the most part nodular and nodulo-ulcerative. The disease can therefore be classed as erythema induratum. However, large nodules which have broken down are also present, and these are really examples of nodular tuberculosis of the hypoderm. In addition, on the left forearm, there is a group of dry scaly papules which under pressure with the diascope are characteristically apple jelly in color. Obviously, three different types of cutaneous tuberculosis are represented in this one patient, and while the condition could be referred to as an unusually extensive example of erythema induratum, it seems to me that to refer to it clinically as tuberculosis of the skin or tuberculosis cutis is more in keeping with present-day nomenclature. The findings in this case do, as Dr. Shaffer said, demonstrate the futility of attempting to make sharp clinical differentiations in the varieties of tuberculosis as it involves and invades the skin. The examination of the chest and tuberculin tests did not show evidence of tuberculosis.

A Case for Diagnosis. Presented by Dr. Robert C. Jamieson.

S. R., a Polish man aged 35, unemployed, has an irrelevant past history. He presents bilateral symmetrical areas of dermatitis on the thenar portion of the

palms, and a similar eruption extends from the central portion of the soles to the internal malleoli. All the involved areas have sharply demarcated borders and the entire involved surfaces are studded with small, deep pustules which have gradually dried and become exfoliated. Pruritus is absent or only slight at times. The lesions have been present for two years. Examination of scrapings from the pustules did not show any fungi. The reaction to trichophytin was positive. The patient has received local treatment and roentgen irradiation for tinea of the hands. My suggestions as to the diagnosis are: (1) tinea, (2) acrodermatitis of Hallopeau, (3) pustular psoriasis.

DISCUSSION

DR. CHESTER A. DOTY: Were slides made to determine the presence of actinomycosis?

DR. LOREN W. SHAFFER: I think that this condition has been described recently (Mitchell, J. H.: Dermatitis Herpetiformis [?] with Recurrent Vesicopustular Lesions on Palms and Soles, ARCH. DERMAT. & SYPH. **29**:128 [Jan.] 1934). All methods of investigation in this case did not lead to a diagnosis. The question of a relationship to pustular psoriasis and acrodermatitis is thoroughly discussed. Therapy has usually been futile in such cases. I believe that the article referred to does not substantiate the fact that these cases fall in the group due to Monilia. I have had fairly good success with local application of silver nitrate. Application of tar often produces satisfactory results. I had a patient who used tar successfully.

DR. HOWARD J. PARKHURST: Because of the sharp outline of the involved areas extending from the ankle to the soles, the small vesicular and not pustular lesions which I found in these areas and the negative results of cultures and of examination of slides, I have to make a diagnosis of dermatomycosis or infection with Monilia.

DR. CYRIL K. VALADE: I agree with Dr. Parkhurst.

DR. ROBERT C. JAMIESON: I presented the patient for diagnosis and suggestions for therapy. During the last two years I have had several patients with this condition and with most of them I have gotten just about as far as this. The condition improves to a certain point and then remains stationary, no matter what is done. This man has been treated for ringworm for a long time. He had extensive roentgen therapy with little or only temporary benefit. When I made the scrapings I took almost an entire vesicle. The trichophytin test was positive, and the test with oidiomycin was negative. We are right back where we started. The same type of pustular lesions developed in one of the patients whom I had treated for a long time with the usual roentgen method, and that patient got well on a dietary regimen. She says the only thing she did was to change her diet. It seems to me that these manifestations are due to more than ordinary ringworm. This man says that no itching is present. He has a large number of pustules. Recently he has received the treatment with potassium permanganate and other therapy usually administered to patients with ringworm. I do not know whether this condition represents an unusual form of pustular psoriasis, whether it is acrodermatitis, whether it is an infection with ringworm or Monilia or whether it is a form of toxic dermatitis due to some focus of infection.

DR. WILLIAM G. WANDER: Were cultures on Sabouraud's medium made?

DR. O. M. GRUHZIT: I wish to add a comment. The lesion is vesicular. In working in the laboratory chemicals, such as concentrated nitric acid, are used to dry up the lesions. It is a heroic treatment, but it is not painful.

A CASE FOR DIAGNOSIS (PSORIASIS, FUNGOUS INFECTION, ENDOCRINE DISTURBANCE?). Presented by DR. ROBERT C. JAMIESON.

F. A., a man aged 43, whose family and past history are irrelevant except for an attack of syphilitic urethritis in 1930, presents the following conditions: an elevation of the distal border of several nails of the hands and the nails of both great toes by accumulation of scales under the free border and a gradual destruc-

tion of the nail toward the proximal end, two rounded reddened and scaly psoriasiform patches on the left knee and leg and several small lesions of keratoderma on the left sole. The nails have been treated with local applications and roentgen irradiation for fungous infection.

The initial lesion, which appeared one year ago under the distal border of the left index finger, consisted of a small area of undermining with accumulation of scale. Paronychia and arthritis of the distal joint on that finger subsequently developed.

The possibility of psoriasis, fungous infection, endocrine disturbances or keratoderma blennorrhagicum have been considered. No examinations for fungi have been made recently.

DISCUSSION

DR. G. WARREN HYDE: In my opinion this man shows a definite focus of dermatomycosis of the nails. He did not have much interdigital peeling, but I think that this is a clearcut case of dermatomycosis. I regard the thickened scaly lesions as the hypertrophic type of dermatomycosis.

DR. HARTHER L. KEIM: I hardly believe that a diagnosis of keratoderma blennorrhagicum can be established in this case. There is a gradual accumulation of cheesy material beneath the nails, and the nail plates themselves are not heaped up until quite late in the process. In addition, I believe that if keratoderma blennorrhagicum caused the condition in the nails the cutaneous lesions would be more extensive and perhaps more typical. I doubt whether it is possible to establish a clinical diagnosis at this time, but I favor the diagnosis of dermatomycosis.

DR. ROBERT C. JAMIESON: I saw the patient for the first time yesterday. He has been under treatment for dermatomycosis for some time, but no definite results have been obtained. The patient told me that small yellowish lesions developed at the proximal end of the nail and that a cheesy material such as can be seen extending way back under the nail appeared. When I first saw the nails, I hardly knew what clinical diagnosis to make. I think that probably the patient has psoriasis of the nails. Psoriasis of the nails alone occurs infrequently. It is difficult to make a diagnosis of psoriasis of the nails unless there are additional symptoms. In spite of the fact that the condition has progressed for two years the nails on two of the affected fingers show no symptoms of a mycotic infection. The nails are long, as in psoriasis. My impression was then, and it will be until I have found other evidence, that this is a case of psoriasis of the nails. As for the two lesions on the legs, I think that they are likewise psoriatic.

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## NEW YORK DERMATOLOGICAL SOCIETY

R. H. RULISON, M.D., *Secretary*

*Regular Meeting, Dec. 18, 1934*

FRED WISE, M.D., *President*

ACAROPHOBIA. Presented by DR. F. C. COMBES.

L. M., a woman aged 29, was first seen by me about two weeks ago. She was accompanied by her brother who, like the other siblings, namely, three sisters, has the same complaint as the patient. For the last three months the patient has had a generalized pruritus which she ascribes to infestation with a mite. She has removed from her arms small black particles which, under the microscope, proved to be coal dust. At one time she presented two particles on the palm of one hand, one of which was over a millimeter in diameter and was easily brushed off. There is no evidence of itching and no dermographism. She has applied

numerous remedies given her at various places, and she admits that nothing any physician tells her to the contrary will convince her that the particles are not parasites.

DISCUSSION

DR. H. H. WHITEHOUSE: I agree absolutely with the diagnosis from the investigation I made of the spots. The way the phobia spreads through the family is pathetic.

DR. CHARLES MALLORY WILLIAMS: I agree with the diagnosis, and the fact that the patient states explicitly that she would not give up her belief even if all the specks were examined and it was proved that they were not parasites shows how serious and fixed the obsession is. I advise that she be sent to a psychiatrist, who is more competent to treat that kind of illness.

DR. HOWARD FOX: Although I think there is no doubt about the presenter's diagnosis, it is possible to be mistaken in such cases. This happened in the case of a woman I saw who acquired an infestation of lice in the Orient. She was promptly relieved of this disease, but later she suffered again from generalized itching and complained that the infestation had not been cured. She showed an envelop containing little black specks, one of which on careful examination was seen to move. Under the microscope this proved to be an arthropod with eight legs; hence it was not a pediculus or other true insect. The parasites were evidently tiny spiders which had gotten on the patient's clothes from the shrubbery near her house. The spiders were shown to a member of the staff of the Museum of Natural History, who identified the exact species. The patient was entirely satisfied to have the proof that the parasites were not lice.

DR. E. R. MALONEY: I agree with the diagnosis and also with the recommendation of Dr. Williams.

DR. FRED WISE: I have had an experience similar to that mentioned by Dr. Fox. In some cases of eruptions and symptoms which at first sight seem to point to acarophobia, further investigation may prove the condition to be an infection with the mite of canary bird scabies. Two or three patients with such a disease were successfully treated at the clinic of the Post-Graduate Medical School and Hospital.

DR. HOWARD FOX: There is a mite, Dermanyssus avium et gallinae, which infests poultry and which at times attacks man.

LICHEN PLANUS CONFINED TO THE MOUTH. Presented by DR. HOWARD FOX.

Mrs. B. S., a stenographer aged 30, first noticed the eruption while looking at her tongue in a mirror three months ago. At no time have there been any subjective symptoms. The eruption is profuse and situated on the mucous membrane of the cheeks, on the dorsal and inferior surface of the tongue and on the gums. It consists of numerous grayish-white pinpoint dots, circles, streaks and an interlacing meshwork. A slight infiltration is perceptible on palpation. On the dorsum of the tongue the lesions consist of several diffuse patches the size of a small coin. The patient would not submit to a general examination, but she is sure there are no cutaneous lesions. The teeth are in excellent condition. She drinks little alcohol and smokes a cigaret only occasionally. She has no digestive disturbances but is fond of eating highly spiced food. The Wassermann reaction was negative. The patient has received no treatment.

DISCUSSION

DR. R. H. RULISON: I think there is no doubt that the diagnosis is correct in this case.

DR. FRED WISE: All the members, I think, agree with the diagnosis.

DR. CHARLES MALLORY WILLIAMS: The lesions on the tongue are the most interesting to me. I think they are those of lichen planus. I agree with the diagnosis, but if lesions like those at present on the tongue only and there are no

lesions on the cheeks the diagnosis is difficult. I have had two patients with such lesions under my care for years, and the condition has never spread. I cannot make any other diagnosis.

DR. A. BENSON CANNON: I think that Dr. Fox's diagnosis is correct and I believe that lichen planus confined to the mucous membranes is more common than one realizes. Most of the dental surgeons, I think, see these patients first and then refer them to physicians. During the past fifteen years I have seen a large number of cases of lichen planus of the mouth. In some of the cases which I have been able to follow lesions have developed subsequently on the genitalia. If this patient has not already been examined for lesions of the vulva and rectum I should think it would be of interest to know whether she has papules of lichen planus there too.

DR. H. H. WHITEHOUSE: I was about to assume that Dr. Fox examined the vulva and found no lesions. Probably he has, but the remarks that Dr. Cannon has made absolutely fit a case of lichen planus which I have observed. In that case I thought that the lesions were exclusively confined to the mouth. The patient had an advanced eruption of lichen planus of the vulva but no lesions on the skin; only the mucous surfaces of the vulva were involved. In my case the eruption did not involve the rectum as it did in that to which Dr. Cannon referred. It was located only in the buccal cavity and the vulva.

DR. J. J. ELLER: I agree with the presenter's diagnosis. I should like to know whether he has the same impression that I have regarding the management of these cases. I understand that the disease never becomes malignant and that the lesions produce no systemic symptoms, and it is my impression that it is better not to give any treatment. I have heard of only one case in which malignant degeneration and death occurred, that of a patient in New York who received, I believe, too much radium therapy for lichen planus of the mouth. As far as I know in no other case has lichen planus of the mouth resulted in malignant degeneration and death. It would be better, in my opinion, to leave this condition untreated.

DR. HOWARD FOX: I am glad that the members agree unanimously with my diagnosis, as I had a hard time several years ago to convince some of the members that the disease might be confined to the mouth. Seven of the patients whose cases formed the basis of my reported series of ten such cases were presented before this society, and in six cases the diagnosis was proved histologically (Fox, Howard: Lichen Planus Confined to the Mouth, ARCH. DERMAT. & SYPH. **24**:1071 [Dec.] 1931). In this case I did not think it necessary to perform a biopsy to confirm the diagnosis.

I agree entirely that when the disease is confined to the mouth the treatment, whether local or general, is unsatisfactory. In one of my cases the eruption had lasted for eight years and it improved when the patient temporarily discontinued smoking. In another case there was a complete disappearance of the eruption after the patient on her own initiative had painted the patches with iodine. This may have been a coincidence as I tried this method later in other cases without any success.

CHONDRODERMATITIS NODULARIS AURICULARIS. Presented by DR. F. C. COMBES.

P. O., a man aged 58, presents on the upper crux of the anthelix of the left ear an ovoid nodule 10 mm. in diameter, with a depressed scaly center firmly attached to the cartilage beneath. The lesion is tender, which makes it impossible for the patient to recline on that side. It may be noted that the shape of the patient's ear makes the anthelix more prominent than the helix. When the lesion was first seen, in January 1931, it had been present for two months. It was treated with 2 erythema doses of roentgen rays on three occasions at intervals of two months without effect. It was then widely removed by endothermy and curettage. Nine months later it recurred and was treated on two occasions with lightly filtered radium, a total of 30 mg. hours being given. This was in November 1932. The treatment produced no appreciable effect. Since that time the lesion has remained stationary.

DISCUSSION

DR. A. BENSON CANNON: I think it is unusual to see this condition in a man, although I have frequently seen it in women, especially since they began to wear their hats down on one ear. I had always attributed the condition to trauma or long-standing irritation from pressure resulting from the hairpins or hat. I have had more success by removing the lesions by electrosurgery than by any other method. I think that that treatment is preferable to the use of roentgen rays or radium because, I believe, roentgen or radium therapy may result in what this man presents at the moment, that is, the effects of too much radiation, a thing perhaps less desirable than the original lesion.

DR. H. H. WHITEHOUSE: I agree with the diagnosis and the therapeutic suggestions as expressed by Dr. Cannon.

DR. EUGENE F. TRAUB: Contrary to the usual experience, all the patients that I have seen with this condition have been men. As I have encountered at least a half-dozen or more cases in men, none of whom wore ear-muffs or hats pressing against the affected area, the theory expressed by Dr. Cannon certainly does not account for all cases. What Dr. Cannon has said about therapy fits in exactly with my own experience.

DR. J. J. ELLER: I agree with Dr. Cannon that it is far better to destroy these lesions by means of some surgical procedure than to apply large doses of radiation. Most of the cases I have seen have been in women.

DR. FRED WISE: I agree especially that the therapy should not consist of roentgen rays or radium when the cartilage of the ear is already involved. I believe that electrodesiccation or electrocoagulation is indicated.

DR. F. C. COMBES: In the majority of cases this disease seems to occur in women, and in all the cases I have observed the lesions have been on the helix. This is the first case in which I have seen any on the anthelix. In all my other cases there has been satisfactory response to electrosurgery and curettage. I treated one lesion successfully with carbon dioxide snow. As I said before, in the present case I destroyed the nodule entirely with electrocoagulation, curetted the area all out and went quite deep. The wound healed, and the nodule promptly recurred. I think that I shall try treatment by excision. Such lesions have been excised and have returned after excision.

BROMODERMA. Presented by DR. J. J. ELLER.

R. M., an Italian man aged 47, presents a well defined, palm-sized ulcerated lesion on the anterior middle surface of each leg. There are several pea-sized erythematous papules and papulopustules scattered over the face and back. The condition is of three weeks' duration, and about 35 per cent improvement has occurred in the past week as a result of intravenous injections of sodium chloride. The patient has epilepsy, and for the previous four weeks he has taken a preparation called "donhide" which has been found to contain bromides, iodides and chloral.

DISCUSSION

DR. E. R. MALONEY: I agree with the diagnosis.

DR. F. C. COMBES: The clinical picture conforms to what one might expect from a retention of bromides and iodides.

DR. EUGENE F. TRAUB: I also agree with the diagnosis, but I believe that the eruption has been there a little longer than the history appears to indicate. A few years ago I saw a woman who had on both legs a somewhat more extensive eruption due to bromide in which granulomatous tumors had formed. She had been to several hospitals and dispensaries, and a diagnosis of malignant degeneration had been made on one of the large fungating lesions. Amputation of the leg had been recommended. Fortunately for her, this had so frightened her that she

visited several physicians until the true nature of the condition was recognized. A few injections of sodium chloride brought about a complete disappearance of her lesions.

DR. R. H. RULISON: I think that the patient has an eruption due to ingestion of bromide.

DR. H. H. WHITEHOUSE: I agree with the diagnosis, and the location on the legs is confirmatory. I have had two cases such as that referred to by Dr. Traub in which the condition was thought to be due to a fungus, and in two other cases the patients were advised to have an amputation because of sarcoma. In all these cases the lesions cleared up when the use of the bromides was discontinued.

DR. CHARLES MALLORY WILLIAMS: I agree that this is an eruption due to bromide, and I think that it has been present a good deal longer than three weeks.

DR. HOWARD FOX: I should qualify Dr. Williams' statement and say that this is an eruption due to either a bromide or an iodide. It looks more like an eruption of the bromide type, but it might be either. I have a photograph of the granulomatous type of eruption suggesting blastomycosis or tuberculosis verrucosa which was caused by taking large doses of iodides for three months. A point in the diagnosis that has not been mentioned is the pain and tenderness that frequently accompany bromoderma or iododerma. I also think that the patient must have taken the drug much longer than four weeks, for that is a short time for this type of eruption to develop. He has doubtless taken the medicine for several months at least.

DR. J. J. ELLER: I think the history is difficult to obtain in these cases, particularly when the patient does not speak English. However, this patient was treated for epilepsy in St. Luke's Hospital about four weeks ago. He had no eruption then. I should not be surprised to find that he was then given bromides for that condition. I have found that an eruption due to iodide can so closely simulate an eruption due to bromide that it is difficult to differentiate the two conditions.

DERMATITIS VENENATA (DUE TO CEMENT). Presented by DR. J. J. ELLER.

P. B., an Italian man aged 48, is a cement worker. He was first seen by me on Oct. 29, 1934, at which time he presented on the dorsa of the hands, dorsal and palmar surfaces of the forearms, front and sides of the neck, nose, area below the eyes and forehead an eczematous, scaly, weeping, intensely reddened eruption with minute vesicles and some crusting. As the patient can speak only Italian, it was necessary to employ an interpreter to obtain a history. The only definite information obtained in the history was that a great deal of pruritus was noticed when the patient was at work. He has used several types of cream in attempting to cleanse the skin. He uses no soaps at work. According to the history, cement was suspected of being the etiologic agent.

Patch tests were made with cement in solution and in a cream base, and the test substances were applied on the back first. These tests proved negative. Then the same test substances were applied to one forearm, in the belief that possibly the condition was a localized sensitivity. At the same time patch tests were made with the creams the patient used. All the patch tests were negative. As it was still believed that cement was the etiologic agent, the patient was asked to inhale the dust caused by stirring dry cement two or three times during one day and to return for observation the next day. On his return the next day, his condition was exactly the same as the first day. He was then told to apply dry cement to one forearm and to return the next day for observation. An acute exacerbation of his former condition was present on the area on the forearm to which the cement had been applied. The other arm, which was used as a control, was unchanged. Patch tests were then made again on the back and arm and proved negative.

The most interesting features about this case are: (1) localized sensitivity to cement with negative reactions to patch tests on the back and on the affected area; (2) negative reactions to all tests with substances other than cement; (3) sensitivity from inhalation, causing dermatitis on the forehead, under the eyes and on the nose, and (4) reaction obtainable only by application of dry cement to the area of sensitivity; negative results from tests with solution and ointment containing cement.

DISCUSSION

DR. CHARLES MALLORY WILLIAMS: I agree with what has been said, and I think it is well to emphasize the importance of the fact that a localized sensitivity exists. Otherwise one is likely to be deceived in making a patch test. It is important to remember this because a negative reaction to a test made on another part of the skin leads to a false conclusion.

DR. EUGENE F. TRAUB: I treated a cement worker off and on for three or four years. He was subjected to repeated patch tests with wet and dry cement and with various chemicals. The patient believed that a chemical which had been put into the cement during the process of mixing to make it set quickly was the cause of his dermatitis. There is some question as to whether this was actually the cause, as he appeared again a few days ago with a new eruption which developed while he was working on another job and handling cement in which no such chemical was used. The patch tests had been made on portions of the forearms as close as feasible to the affected areas. It is possible that patch tests made in the ordinary routine manner with cement, even in persons susceptible to a dermatitis caused by cement, may not elicit a positive reaction; this may be due to the fact that the material should be rubbed in, friction being the important point. There is no question as to the clinical diagnosis either in the case of the patient presented or in that of the patient to whom I referred.

DR. F. C. COMBES: I do not understand the classification of this case or the course of events. As I understand it, there were negative reactions to the patch test in the unaffected areas and in the affected areas on the arm. Was a patch test made on the forehead, and if so was the reaction to that test positive? Moreover, the history states that this dermatitis developed on the face when cement was inhaled. The presenter surely does not really mean inhalation. There was probably a local contact of the cement with the forehead during the process of stirring up the cement in the bag. Still a dermatitis did not develop on the affected areas of the arm when the cement was applied to the arm. I cannot understand why the condition should develop on the face and not be aggravated on the arm when patch tests were made on areas already affected by the dermatitis.

DR. FRED WISE: I am much interested in a case of this kind because I have great difficulty in submitting satisfactory opinions on dermatitis caused by cement to the insurance companies. I should like to hear from Dr. Traub as to the chemical constitution of the material used to quicken the process of setting.

DR. EUGENE F. TRAUB: Unfortunately I am unable to give the exact chemical formula. I doubt whether I have it at my office. I tried to find out at the time exactly what was added to the cement, but either no one knew the exact nature of the solution or its composition was changed from time to time; the nature of the ingredients was not known or information was purposely withheld. I could never determine the real facts. Whatever the ingredient was, it was added to the cement to make it set quickly, particularly in cold weather.

DR. FRED WISE: Did Dr. Traub's patient acquire the dermatitis when he handled cement not containing the setting chemical?

DR. EUGENE F. TRAUB: Yes, he did.

DR. R. H. RULISON: Is it possible that the eruption is caused by irritation of the skin due merely to the sharp points on the particles and not to the chemical properties of cement?

DR. CHARLES MALLORY WILLIAMS: Was the patch test made on the affected area of the hands, that is, on the skin already diseased, and if so did it not produce any increase of the eruption?

DR. J. J. ELLER: I presented this patient for the reason which Dr. Williams discussed. The lesions flared up locally after the cement was rubbed on, and there was a flaring up of the dermatitis on the face after the so-called inhalation when the cement was stirred up in a bag and the patient put his face over the bag to inhale. The patch test was negative. There are many cases of occupational dermatitis or dermatitis venenata known to be due to a certain substance in which patch tests give negative reactions. The reason is difficult to explain. Probably the only way to prove the origin of the dermatitis is to have the patient get well and again expose him to the irritant or have him rub it in on the areas which were affected.

DR. R. H. RULISON: Unless I am mistaken, pastry bakers acquire a dermatitis which is supposed to be due to the sharp particles of powdered sugar which they use, whereas bread bakers never get that type of dermatitis. The injury is largely mechanical. I wonder whether the cement dermatitis is not merely traumatic like the condition resulting from the use of sandpaper. If sandpaper is rubbed into the arm, a dermatitis results, but the patch test with sandpaper is negative. Pastry bakers mix flour or dough with powdered sugar and acquire a dermatitis, but the patch test is negative. Is this not a possible explanation for this case?

DR. J. J. ELLER: How does Dr. Rulison's mechanical theory account for the eruption on the face from the so-called inhalation?

A CASE FOR DIAGNOSIS (PAPULONECROTIC TUBERCULID?). Presented by DR. EUGENE F. TRAUB.

W. B., a man aged 57, born in the United States, has an eruption of several years' duration which involves particularly the extremities. The forearms and thighs present most of the lesions, although scattered areas are found on the lower portion of the leg, upper portions of the arms and dorsa of the hands. The trunk is free from lesions. In addition to the eruption because of which he is presented, the patient also shows a vesicular eruption of the palms and soles which has been clinically diagnosed as a dermatomycosis, although repeated examinations and cultures have failed to reveal fungi. On the dorsum of the hand, especially over the fingers, are a number of papular lesions with necrotic centers. On the forearm there are clusters of lesions which seem to be papulopustular, the pustular element disappearing to leave crusts and, when complete healing has taken place, scars. On the thighs there are similar lesions, but there some of the groups seem to show a horseshoe-shaped configuration or at least a grouping of segments of an incomplete circle. Several of these lesions slightly resemble a lesion of tertiary syphilis. At the onset, the possibility of an eruption due to a drug was considered, but no history to that effect was obtained. The Wassermann, Kline and Kahn tests have been negative, and two biopsies have been reported on as follows: The section of the first specimen showed a fairly normal epidermis. There was slight dilatation of the blood vessels in the upper part of the corium. The blood vessels were surrounded by a slight infiltration which was in islands and bands. In the middle part of the corium, down to just above the coil ducts, there was marked degeneration of the connective tissue fibers. They had lost their normal contours, and the deeper areas took on a basophilic tinge. There seemed to be some edema as well. The exudate consisted of lymphocytes. The picture was similar to that often seen in nontuberculous granuloma annulare.

The section of the second specimen showed islands of cellular exudate in the corium. These were seen even about the coil glands. The exudate was perivascular and consisted of lymphocytes and occasional endothelial cells and giant cells. The endothelium of the blood vessels was swollen. Some of the blood vessels were engorged, and some hemorrhage had occurred even in the upper part of the

corium. There was a large amount of intracellular and extracellular edema. Some of the edema was present in the epidermis as hydropic degeneration. There were hyperchromatic nuclei in this area.

DISCUSSION

DR. HOWARD FOX: Among the various diagnoses suggested I should certainly exclude syphilis on clinical grounds alone. The lesion has none of the earmarks of an eruption of late syphilis, such as grouping, asymmetry and sharp demarcation of the patches. I did not see much that was indicative of granuloma annulare and saw none of the characteristic pitted scars of papulonecrotic tuberculid.

DR. E. R. MALONEY: I agree with Dr. Fox's statement about syphilis and papulonecrotic tuberculid and about granuloma annulare. I do not see how one can make a definite clinical diagnosis of any one of those three conditions. I do not know what the basis of this eruption is. It may be a rash from the dermatomycosis, but the eruption has been changed considerably by the patient's picking at it. He certainly has dug at some of these lesions, and this has produced a good deal of the picture that exists now. I should not make a positive diagnosis, but the eruption certainly does not look to me like a tuberculous condition or a tuberculid or like syphilis.

DR. F. C. COMBES: I agree with Dr. Maloney.

DR. R. H. RULISON: I think this is a puzzling case. Clinically, in spite of the symmetry of the eruption and in spite of the negative results of laboratory examinations, I got the impression that this eruption is a late syphilid. It seems to me that the nodules lying directly under the skin of the forearm strongly suggest subcutaneous syphilitic nodules.

DR. J. J. ELLER: I cannot consider this patient's eruption as a papulonecrotic tuberculid or as syphilitic lesions.

DR. H. H. WHITEHOUSE: I agree with Dr. Eller.

DR. A. BENSON CANNON: If the previous speakers had not so positively opposed the diagnosis of papulonecrotic tuberculid and granuloma annulare, I should have suggested these diagnoses. This patient has papules and nodules on the dorsa of the hands and also on the sides of the fingers and dorsa of the feet. Many of the lesions have necrotic and depressed centers. Those on the thighs are annular to circinate, infiltrated and hard. The only things that make me hesitate to call the latter lesions nodules of granuloma annulare are the redness of the skin over them and the abrasion of the epidermis which might be attributed to treatment or to rubbing. I think that in view of the location, the chronicity and character of the lesions and the histologic picture, I should class the condition in the paratuberculid group.

DR. CHARLES MALLORY WILLIAMS: I agree with what Dr. Fox said as to ruling out syphilis. I cannot see anything suggestive of syphilitic lesions in this patient's eruption. I can see no excuse for calling it a trichophytid. I am tired of that diagnosis. In my experience the only cases of trichophytid which would produce destruction such as that exhibited by this patient occur in acute trichophytosis, and the lesions are large, nodular and red. They look more like blastomycosis than this does. The patient may have tinea. I did not look at his feet to see whether signs of tinea were present. I think that the whole discussion as to chronic trichophytid is erroneous. Acute trichophytid I can recognize. I cannot see any excuse for calling this a trichophytid unless some one can show me the organisms, and I do not think that any one can do that.

I should like to emphasize what Dr. Cannon said. The lesions on the hands are of the early type. On the thumb and tips of the fingers are small, firm, round lesions, not red. They are in the early stages. In the early stage the lesions are pale. Later depressions tend to form in the center, and sometimes there is slight scaling. There are several of those lesions on the hands. If they were seen without the rest of the picture, they would be called nodules of granuloma annulare, and that, I think, is the correct diagnosis. The lesions have spread, and my

impression, although I cannot be certain about this, is that the older and larger lesions represent the same process, altered by irritation and probably aberrant from the usual type. One does not know what granuloma annulare is. That disease can best be explained as a reaction of the skin due to some sort of bacterial irritation, and the condition may be classed in the same group as papulonecrotic tuberculid. I do not see why one cannot accept intermediate types such as are shown in this case. I think that the condition belongs in the group I have mentioned.

Dr. F. C. Combes: I wish to make a suggestion. I think that graded tuberculin tests would be useful. If the eruption is a papulonecrotic tuberculid it should show considerable resistivity to tuberculin.

Dr. Fred Wise: The impression I had was the same as that expressed by Dr. Cannon and the presenter, namely that this patient has a papulonecrotic tuberculid of the nose and the feet. The lesions on the legs and thighs seem to me to be a form of true tuberculosis or possibly sarcoids. I could not see the resemblance to lesions of granuloma annulare. I believe that further investigation will reveal that all the lesions are of a tuberculous nature. I certainly should rule out syphilis and ringworm. I therefore agree with the presenter's diagnosis.

Dr. Eugene F. Traub: The early discussion on this case reminded me much of the way I felt each time I saw the patient during his first few visits to the hospital. The picture seemed to change each time so that it was difficult to ascertain the exact character of the lesions. Now that I have followed him for some time I feel certain that a diagnosis of syphilis can be excluded in spite of the fact that some of the lesions on the thigh have a configuration and appearance suggestive of a nodulo-ulcerative syphilid. I believe that the patient has a coincidental dermatomycosis, although repeated examinations and cultures were negative for fungi. However, the tiny vesicular lesions on the hands and feet have no bearing on the rest of the picture. As nearly as I was able to do so, I have excluded the possibility of an eruption due to drugs, although I was surprised that no one suggested that diagnosis. When the patient was first seen the condition closely simulated a pustular eruption due to bromide or iodide. After I finally had excluded one diagnosis after another I felt that this was some type of cutaneous tuberculosis or a tuberculid, but I was not absolutely certain as to how to classify it. Some of the lesions on the hands were distinctly papular with necrotic centers, and for this reason the diagnosis of papulonecrotic tuberculid was made.

Generalized Erythroderma (Mycosis Fungoides?). Presented by Dr. Howard Fox.

H. F., an American aged 25, a plumber, first noticed the eruption nine and one-half months ago. He has never shown any clinical evidence of lead poisoning. He was first seen by me six months ago, at which time he was suffering from an exfoliative dermatitis which was almost universal. There was no history of ingestion of drugs or injections of foreign protein before the onset of the eruption. When the patient was first seen there was no appreciable enlargement of the lymphatic glands. The patient went to the Bellevue Hospital, where routine laboratory examinations, including the Wassermann test, red and white blood cell counts, differential count and urinalysis, showed nothing abnormal. A single examination of the urine was negative for arsenic and lead. No improvement resulted from injections of sodium thiosulphate. The condition improved, however, after the patient took iron and ammonium citrate for a month. After he left the hospital he was given forty-two injections of sodium arsenate by his family physician. During the latter part of this course of treatment (several weeks ago) he noticed a change in the type of the eruption on the trunk. In the locality where the original scaling erythroderma had previously cleared up considerably, he noticed discrete small "lumpy" patches. These lesions are decidedly infiltrated, red and more or less scaly. There are, however, none of the bizarre configurations characteristic of mycosis fungoides. Yesterday a biopsy on one of these infiltrated

patches and a sedimentation test of the blood were made. The rate of sedimentation was 70 mm. in one hour. At present the femoral and inguinal glands are moderately enlarged, and the axillary glands are markedly enlarged. The patient is a tall, well nourished, vigorous-looking man.

DISCUSSION

DR. R. H. RULISON: I think this patient's eruption is suggestive of an early mycosis fungoides.

DR. EUGENE F. TRAUB: I doubt whether it is possible to make a positive diagnosis at this stage of the eruption, but I believe that if the condition belongs in the lymphoblastoma group the case should be studied particularly with the thought that the disease might be leukemia rather than mycosis fungoides. The fact that on one occasion early in the process the blood picture was normal does not exclude the diagnosis of leukemia.

DR. F. C. COMBES: I agree with what the previous speakers have said. The patient probably has a beginning mycosis fungoides.

DR. CHARLES MALLORY WILLIAMS: I think the disease is mycosis fungoides.

DR. J. J. ELLER: I am inclined to consider the possibility of mycosis fungoides.

DR. A. BENSON CANNON: I think that any generalized dermatitis which is extremely pruriginous should be considered in the light of granuloma fungoides, but in this case I am much more impressed with the possibility of simple dermatitis. I did not see any of the configurations which are usually present in cases of granuloma fungoides. There is altogether too much dermatitis, and the lesions show entirely too much inflammation, edema, vesiculation and crusting to justify a diagnosis of granuloma fungoides. I think that the enlargement of the glands is entirely in keeping with a diagnosis of a simple inflammatory condition of the skin. Furthermore, I should attach no importance to a negative report of an examination of the urine for arsenic. I believe that the evidence of a true retention of arsenic is to be gained from an examination of the blood and not from a study of the urine. In my opinion, if a man is excreting arsenic in quantities sufficient to be evident in the urine he is all right, but I think that the man who is retaining his arsenic in the blood without showing any in the urine is the one who is in the dangerous situation. I should want further evidence that this patient's condition is not a metallic poisoning, especially as he is a plumber.

DR. FRED WISE: The impression I have is similar to that expressed by Dr. Cannon. I do not think that this patient has mycosis fungoides because the clinical changes are as yet insufficient to justify that assumption. I think that the conventional treatment which is directed against dermatitis rather than against any granulomatous formation or disease of the blood will eventually effect a cure in this man. I also realize that the so-called *homme rouge* stage precedes mycosis fungoides, but I do not think that this is that kind of prefungoid eruption.

DR. HOWARD FOX: The varying opinions expressed reflect my state of mind in trying to make a diagnosis. Mycosis fungoides is merely one of the possibilities in view of the recent apparent change in the type of eruption. The lumpy lesions have developed lately and have no relation to the diffuse scaly areas. The eruption does not show the classic changes of an eczema. Until recently the eruption had the appearance of an exfoliative dermatitis. As to arsenic, it would not be proper to make an examination for this metal at present, as the patient has recently received sodium arsenate. Incidentally, it has done him no good.

MULTIPLE NEVI OF VARIOUS TYPES. Presented by DR. E. R. MALONEY.

J. W., a man aged 51, born in Lithuania, presents a verrucous eruption on the dorsum of each foot; in places the lesions resemble ichthyosis. Both legs show lesions of keratosis pilaris, and on the extensor surfaces of both forearms are areas of hyperkeratotic skin. On the trunk there are numerous pigmented nevi and seborrheic warts.

The eruption on the feet and forearms has existed since the patient's birth. The father and one brother of the patient have the same condition. The patient's father has one brother who is not affected and whose two children are not affected. The patient himself has no children. The patient's brother who is affected has three children who are not affected. The patient has two other brothers and one sister who show no evidence of the disease.

DISCUSSION

DR. J. J. ELLER: I should class this condition as a nevus, and I think that the disease is familial.

DR. EUGENE F. TRAUB: Undoubtedly this is some form of nevus, but the patient has a great deal of scaling, a large portion of which, I am sure, would disappear were he to use an ointment containing salicylic acid for a short time. The application of this type of ointment, together with suitable bathing, would give him a great deal of comfort.

DR. HOWARD FOX: There is no doubt that the eruption, including the extensive dryness, keratosis pilaris and the ichthyosis hystrix-like eruption of the feet, is a congenital abnormality of the skin. The interesting point in this case is the familial incidence of the disease.

DR. CHARLES MALLORY WILLIAMS: There is no doubt about the diagnosis. The point that interests me is the relationship of these various forms of xeroderma. I do not know how many there are—at least a dozen or more. It seems to me one has gone a little too far in giving too many names to slight variations in appearance. This is an exaggerated form of dryness of the skin; that is all there is to say about it.

DR. H. H. WHITEHOUSE: I agree with what has been said. This is a congenital condition of abnormal dryness of the skin with ichthyosiform exaggeration in certain parts.

DR. FRED WISE: The eruption on the feet is related to a form of ichthyosiform erythroderma occurring chiefly on the island of Meleda, in the Adriatic Sea. The hereditary and congenital nature of this type of eruption is linked up with intermarriages in confined communities.

DR. CHARLES MALLORY WILLIAMS: May I ask if there is any history of intermarriage in this family?

DR. E. R. MALONEY: This patient is shown because the familial history is so interesting. Not only does he have the disease, but his father and a brother also have it.

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## CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

*Regular Meeting, Dec. 19, 1934*

JAMES H. MITCHELL, M.D., *President, Presiding*

PEMPHIGUS OF THE ORAL MUCOSA. Presented by DR. E. P. ZEISLER.

A Jewess, aged 53, states that her health was good until August 1934, when soreness of the mouth developed. Vincent's organism was discovered in smears, and for three months the patient was treated for an infection caused by that organism. During that time she lost 25 pounds (11.3 Kg.) and suffered intermittently from fever and chills.

When the patient was first seen by me one month ago the entire mouth showed extensive erosions covered with a yellowish membrane. The lips were swollen and crusted, and there was some enlargement of the submaxillary glands. The

conjunctivae also showed reddening. Under intensive treatment with an arsenical compound administered hypodermically and large doses of viosterol there was rapid improvement, and the oral mucosa was almost healed for about four weeks. Five days ago there was an acute exacerbation with extensive involvement of the entire buccal mucosa consisting of painful erosions and denuded areas. No blisters have been noted on the skin.

A specimen of blood was sent to Dr. Pels for a phytopharmacologic test, but the report had not yet been received.

DISCUSSION

DR. E. P. ZEISLER: There are some lesions on the conjunctiva but none on the skin.

DR. JAMES H. MITCHELL: Has the condition grown worse since August 1934?

DR. E. P. ZEISLER: Yes, the patient has lost 25 or 30 pounds (11.3 or 13.6 Kg.).

HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. JAMES H. MITCHELL.

This patient was presented at the annual meeting of the Dermatological Conference of the Mississippi Valley in January 1934 (ARCH. DERMAT. & SYPH. **30**:282 [Aug.] 1934).

Up to that time the lesions had been limited to the palms. One lesion had been excised, and the section prepared by Dr. Henry Michelson was presented. Since then new lesions have continued to form, and they have yielded to radiotherapy. The patient now has a new lesion on the dorsum of the proximal phalanx of the right middle finger. At present the palms and feet are not involved.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I still maintain that this is a good diagnosis. The small lesions were characteristic histologically when the patient was seen before.

LUPUS ERYTHEMATOSUS OF THE LIP. Presented by DR. A. W. STILLIANS.

This man, a bookkeeper aged 29, states that during the past eight years blisters followed by scales and fissures have appeared at frequent intervals on the lower lip. The lip has seldom been free from these lesions for more than two weeks at a time. The patient also complains of attacks of "hives" about the face and neck which appear several times a year and last only for a few hours.

There are no cutaneous lesions except those of the lip. Three years ago the Wassermann reaction was negative. At that time the basal metabolic rate was normal, although there was a fine tremor of the fingers and the pulse rate was rapid, averaging from 122 to 130 per minute. There was no enlargement of the thyroid gland and no exophthalmos. No history of seborrheic dermatitis, except for slight thinning of the hair at the vertex, could be obtained.

The lower lip is covered with heavy adherent scales and a few crusts. On the inner border of the lip to the left of the center is a crescent-shaped dull bluish-red papule 0.6 cm. long, with fine white lines radiating toward the outer border of the lip. The breath is offensive, possibly because of the presence of several badly decayed teeth.

The blood count showed: erythrocytes, 4,600,000; leukocytes, 8,200, and hemoglobin, 88 per cent (Sahli). The results of the differential count were: polymorphonuclear neutrophils, 63 per cent; small lymphocytes, 30 per cent; large lymphocytes, 5 per cent, and eosinophils, 1 per cent.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I disagree with the diagnosis. I favor a diagnosis of cheilitis glandularis apostematosa. The complete absence of other lesions of lupus erythematosus contraindicates the diagnosis of the presenter.

DR. O. H. FOERSTER, Milwaukee, Wis.: I should be inclined to consider the diagnosis of erythematous lupus, basing it on the presence of the arcuate patch of atrophy, with radiating striae and stippling.

DR. WILLIAM ALLEN PUSEY: Why does Dr. O'Leary specify cheilitis glandularis apostematosa?

DR. PAUL A. O'LEARY, Rochester, Minn.: Because of the apparent hyperactivity of the submucous glands. The mucous bubbles were numerous over the vermilion border, which is the distinguishing differential diagnostic feature between cheilitis exfoliativa and cheilitis glandularis apostematosa.

DR. WILLIAM ALLEN PUSEY: I have become timid about making a definite diagnosis of types of cheilitis. I had an interesting experience with one patient, an intelligent young man, the son of a physician, with cheilitis of many years' duration associated with Fordyce's disease. No treatment was of any benefit, but finally the boy cured himself by taking vitamin D. I think this was not a *post hoc ergo proctor hoc* case; the condition returned after the treatment was discontinued and disappeared again when it was renewed.

DR. UDO J. WILE, Ann Arbor, Mich.: Did not Dr. Stillians say that the present condition was preceded by an eruption of vesicles?

DR. A. W. STILLIANS: The patient said he had "hives" several times a year.

DR. UDO J. WILE, Ann Arbor, Mich.: I was thinking that possibly the present eruption may be the slight atrophy that occurs after multiple attacks of erythema multiforme about the mouth. I do not know of any form of cheilitis preceded by blisters.

DR. A. W. STILLIANS: I am thankful for the discussion. I admit that there is slight ground for the diagnosis of lupus erythematosus, and the history of rapid fluctuation is opposed to it, but the parallel fine white lines on an arciform nodule suggested the possibility.

LICHEN PLANUS. Presented by DR. CLARK W. FINNERUD and DR. RALPH H. SCULL.

This child, aged 9, was presented at the October meeting of the society (ARCH. DERMAT. & SYPH. **31**:735 [May] 1935) because of an eruption on the hands which simulated granuloma annulare but from the microscopic appearance was thought to be lichen planus.

Since that time three lesions have developed at the canthi of the eyes. These lesions consist of pea-sized, annular areas with threadlike, shiny borders and pigmented, clearing centers.

The lesions on the hands have nearly disappeared following three doses (150 roentgens) of roentgen therapy and oral administration of a solution of potassium arsenite.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee, Wis.: As I recall this case, when the patient was originally presented there was some discussion regarding the differentiation between granuloma annulare and lichen planus. The histologic section presented the picture of lichen planus, but clinically the lesions were more suggestive of those of granuloma annulare. I believe that the present lesions on the eyelids are sufficiently characteristic of lichen planus to support that diagnosis for the entire picture.

DR. WILLIAM ALLEN PUSEY: Is the case definitely established as one of lichen planus by the histologic study? On the short examination I made the lesions on the hand look like those of granuloma annulare. The lesion below the eye did look like that of a circinate lichen planus. Lichen planus has taken a place as the great imitator, it seems.

DR. F. E. SENEAR: In one case the eruption completely surrounded the eyes, like an eruption of xanthoma. There was discussion as to whether the disease

was lupus erythematosus or lichen planus, but histologically the picture was that of lichen planus.

DR. CLARK W. FINNERUD: Clinically I still have some doubt as to whether this eruption is lichen planus, although the sections from the lesions on the hand showed as good a picture of lichen planus as we ever saw. The patient has received some roentgen therapy, I think about three treatments, and, although I did not see the child today, I believe the lesions show about 50 per cent improvement. We shall try to get a specimen for biopsy from the lesions on the eyelids.

A CASE FOR DIAGNOSIS (PARAPSORIASIS EN PLAQUES). Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

This man, aged 35, of Russian Jewish descent, presents a generalized maculosquamous eruption of two years' duration which involves the trunk and extremities. He states that the lesions appeared first on the arms and thighs as small, yellowish, erythematous, pruritic macules and that the eruption spread gradually. None of the lesions have disappeared since the onset of the disease.

The results of the general physical examination were negative. The blood pressure was 138 systolic and 100 diastolic. The Wassermann and Kahn tests and the urinalysis gave negative results. Examination of the blood showed: erythrocytes, 4,430,000; leukocytes, 6,500, and hemoglobin, 90 per cent. The results of the differential count were: polymorphonuclear neutrophils, 57 per cent; large lymphocytes, 25 per cent; small lymphocytes, 14 per cent; mononuclears, 2 per cent, and eosinophils, 2 per cent.

In a differential diagnosis parapsoriasis, the premycotic stage of mycosis fungoides and the aleukemic stage of any one of the leukemias were considered.

A microscopic section is presented.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee, Wis.: In view of the mild character of the subjective and objective symptoms accompanying this eruption, which has been present for approximately two years, I favor a diagnosis of parapsoriasis en plaques as opposed to the alternative diagnosis of premycotic stage of mycosis fungoides.

A CASE FOR DIAGNOSIS. (TUBERCULOSIS?). Presented by DR. F. E. SENEAR and DR. MARCUS R. CARO.

This man, aged 39, was in good health until 1929, when hemoptysis due to pulmonary tuberculosis suddenly developed. He spent a year in a sanatorium and was discharged with a diagnosis of arrested tuberculosis with no bacilli in the sputum. During his illness mastoiditis developed on the right side and necessitated an operation. The wound did not heal, and the patient was operated on again in 1931, but the wound still drains occasionally. He states that he has had recurrent attacks of "cold sores" on the upper lip each winter for five or six years but that these lesions always healed without destruction of tissue, as evidenced by the regrowth of his mustache.

In February 1934 he had a sore throat and "cold sores" appeared on the upper lip. Five weeks later, without his having applied any irritants on the skin, the face suddenly swelled, the eyes became puffy and shut and an eruption appeared which spread to the neck and arms. The patient was first seen one week later (March 16, 1934) and at that time he presented intense edema of the upper lip, with several ulcers on the vermilion border covered by a hemorrhagic crust. The face and neck were covered by a dusky red, blotchy and papular dermatitis. On the extensor surfaces of the arms and forearms and on the backs of the hands were many circinate, violaceous brown papules with central vesicular pustules and crusts, typical of erythema multiforme. On the soft palate were several thick, whitish membranous lesions which on microscopic examination showed yeast. There was a large perforation of the anterior portion of the nasal septum.

Physical examination showed evidence of pulmonary tuberculosis with cavitation, and this finding was confirmed by roentgen study. The sputum was negative for tubercle bacilli. The Kahn reaction of the blood was negative.

The patient improved rapidly during his sojourn in the hospital and was discharged after two weeks; the erythema multiforme had subsided; the ulcers were nearly healed, and a mild folliculitis of the bearded region was clearing up rapidly.

Histologic examination of a biopsy specimen taken from the upper lip on May 19, 1934, when there was a slight recurrence of the puffing of the upper lip and of the nose, showed the epidermis to be edematous and flattened by pressure from the underlying infiltrates. The upper part of the corium, right up to the epidermis, was edematous and filled by a densely packed infiltrate of histiocytes, numerous plasma cells, lymphocytes, many eosinophils, and in one area many Langhans giant cells. The blood vessels were widely dilated within the infiltrate and in the underlying tissue. Wide mantles of less edematous but similar infiltration extended down about the deeper vessels, the sebaceous and sweat glands and the hair follicles. No tubercle bacilli were found.

The patient returned on Nov. 30, 1934, with another recurrence of the symptoms, which followed a "cold." This time there was less puffing of the lip and on it were soft reddish-brown, subepidermal nodules varying from the size of a pinhead to that of a pea which on pressure with the diascope had the appearance of apple jelly nodules. Similar small papules were present on the right cheek and right ala of the nose, some being covered by a crust. Scars were present on the nose and upper lip, and on the vermilion border of the right side of the upper lip there was an ulcer covered by a whitish membrane.

Histologic examination of a biopsy specimen taken from the right cheek at this time showed marked edema of the epidermis and corium. The papillae showed fewer changes than the subpapillary and deeper parts of the corium. In these there were large areas of markedly edematous infiltration composed largely of lymphocytes, with few histiocytes and plasma cells. No giant cells were seen, and no tubercle bacilli were found.

DISCUSSION

DR. E. A. OLIVER: This case is similar in many respects to that of a patient I presented about two years ago, a man from the South who had marked involvement of the buccal mucosa and lesions about the chin and cheeks. He was in the Municipal Tuberculosis Sanitarium for about eighteen months; later he was presented before this society with healed lesions on the buccal mucosa and skin. I think this is a case of tuberculosis of the buccal mucosa and lupus vulgaris of the chin.

DR. PAUL A. O'LEARY, Rochester, Minn.: I favor a diagnosis of tuberculosis.

DR. E. P. ZEISLER: I wish to comment on the perforation of the nasal septum in this case. Although this may occur in cases of tuberculosis, it certainly is much more common in cases of syphilis. I suggest the diagnosis of tuberculous syphilid. The histologic picture did not show the classic features of lupus; there were giant cells but not in the definite arrangement seen in tubercles. I think that the entire histologic picture could be explained on the basis of a nodular syphiloderm of the tertiary stage.

DR. FREDERICK R. SCHMIDT: About five years ago I saw a man in the hospital with a septic condition believed to be erythema multiforme. His lip was greatly swollen, and there were some lesions on the face. Later these symptoms disappeared and lesions appeared on the buccal mucous membrane. The condition grew steadily worse, and the patient died one year later. During the entire illness examinations were made repeatedly, and no evidence of tuberculosis was found until the last two months, when Dr. Loewenstein found the bacillus of chicken tuberculosis. This case has been reported, and photographs of the erythema multiforme-like eruption described by Urbach are given. Urbach has classified chicken tuberculosis in four groups; the symptoms begin with small aphthous lesions or with erythema multiforme-like lesions on the lips and in the mouth.

DR. WILLIAM ALLEN PUSEY: Dr. Zeisler's opinion is exactly like mine. The gross appearance of the eruption is that seen in nodular syphilid. Combined with that there is perforation of the nasal septum, which is much more characteristic of syphilis than of tuberculosis. One of the lesions I examined showed a scar which occupied two thirds of the lesions, with a crescent of active process. I should not be satisfied to exclude syphilis until the patient gives a good response to a therapeutic test.

DR. A. W. STILLIANS: In what would the therapeutic test consist?

DR. WILLIAM ALLEN PUSEY: It could be made easily by giving the patient some mercury and then potassium iodide for three or four weeks.

DR. F. E. SENEAR: We have considered the possibiiity of syphilis in this case, particularly in view of the condition of the septum, and we have watched the patient for some time. The thing that does not fit in with either tuberculosis or syphilis is the fact that the eruption starts with a low grade erythema, and overnight a huge edema of the lip and nose may develop, then the picture of erythema multiforme appears. During the last attack the patient was hospitalized, and he recovered within two weeks; hence the therapeutic test would be of no value. He reported occasionally between the last two attacks, and no activity of any kind was noticeable in the lesions. We did not wish to go on record as saying definitely that he has tuberculosis, although from our observations so far we favor that diagnosis much more than that of syphilis. We shall make a therapeutic test, but I do not think that it will permit a definite conclusion.

LYMPHOBLASTOMA. Presented by DR. S. J. ZAKON (by invitation).

This Jewish man, a mattress maker aged 51, states that he has suffered from an intensely pruritic, generalized eruption since June 1932. The condition at no time yielded to local treatment or to superficial roentgen therapy.

On Oct. 18, 1934, he was admitted to the Mount Sinai Hospital. At that time he presented a marked edema of the face, hands and feet, keratoderma of the palms and soles, generalized exfoliative dermatitis, marked lichenification and palpable epitrochlear and inguinal adenopathy. The lymph glands felt hard, and their size varied from that of a hazelnut to that of a walnut, but there was no fluctuation. The spleen was not palpable, and the liver was not enlarged. The temperature fluctuated from 100 to 103 F.

A complete blood count showed 4,000,000 erythrocytes and 80 per cent hemoglobin. The results of the leukocyte count varied from day to day, ranging between 26,100 and 40,400, and the results of differential counts showed from 37 to 77 per cent polymorphonuclear neutrophils, from 8 to 36 per cent eosinophils, from 12 to 34 per cent small and large lymphocytes and from 1 to 3 per cent monoblasts and premonocytes. The chemical examination of the blood gave normal results. There were no parasites in the stools. Cultures of specimens of blood did not produce any growths. No trace of arsenic was found in the urine.

A biopsy of a lymph gland and skin, taken on Oct. 29, 1934, showed a cellular infiltrate in the corium consisting of a variety of cells such as lymphocytes, neutrophilic and eosinophilic leukocytes, many mononuclear and endothelial cells and some large, dark mononuclear cells with clumped, compact nuclei, which resembled the Sternberg-Reid cells.

During the patient's stay in the hospital the febrile period was fourteen days, the fever simulating the Pels-Ebstein syndrome.

In the period of November 5 to December 7 the patient was given eleven doses of roentgen therapy over the entire body. His skin is bronzed and still somewhat infiltrated; the glands, while much smaller than when he was first seen, are still palpable. The leukocytes number 17,900.

The patient is presented as having lymphoblastoma of the mycosis fungoides type, in the premycotic stage.

Biopsy specimens are presented.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: Why is this case classed as the premycotic type rather than as pityriasis rubra of Hebra? Many cases of pityriasis rubra of Hebra were seen formerly and the association that existed between them and leukemia was not recognized. It is a new association, but those patients went along for years without showing evidence of mycosis fungoides.

DR. DAVID LIEBERTHAL: I share the view of Dr. Pusey in regard to the diagnosis of the so-called premycotic stage of mycosis fungoides. The diagnosis of pityriasis rubra of Hebra does not apply to this case either, as in that disease there is no infiltration, the reddened skin shows copious desquamation and gradually there occurs thinning of the skin and pigmentation. The case under consideration will have to be studied over a longer period clinically as well as histologically before a definite diagnosis can be established.

DR. PAUL A. O'LEARY, Rochester, Minn. Do I interpret Dr. Pusey's discussion properly, to imply that he believes a generalized dermatitis may not be a manifestation of mycosis fungoides?

DR. WILLIAM ALLEN PUSEY: I did not say that, but I think it is the case. Mycosis fungoides is a disease which occurs in large areas. In that disorder there may be a generalized dermatitis without any infiltration of the skin, just as in leukemia, but generalized dermatitis in mycosis fungoides is not necessarily of itself mycosis fungoides.

DR. PAUL A. O'LEARY, Rochester, Minn.: Not infrequently mycosis fungoides has been diagnosed by the histologic features of an exfoliative dermatitis, and later the development of a typical clinical picture of mycosis fungoides was noted. It is because of this possibility that a biopsy is made in all cases of exfoliative dermatoses, if for no other reason than to eliminate the possibility of a lymphoblastoma.

DR. WILLIAM ALLEN PUSEY: I have diagnosed a case within the last year on a few spots with pruritus that proved to be lymphoblastomatous infiltration. But I do not think that one would be justified in making a diagnosis of lymphoblastoma in a case of generalized dermatitis in which the patient did not show changes in the blood, or definite histologic changes in the skin.

DR. E. A. OLIVER: My co-workers and I have seen several cases of what was called pityriasis rubra of Hebra at the Cook County Hospital, and in that disease there are a generalized exfoliative dermatitis, distinct atrophy and a small branny desquamation of scales, and the patient suffers from chilliness. This patient has none of these symptoms, and I cannot subscribe to that diagnosis.

DR. WILLIAM ALLEN PUSEY: I agree to that, but neither is the disease what was formerly called mycosis fungoides.

DR. S. J. ZAKON: The pathologist made a diagnosis of Hodgkin's disease, but the histologic picture in the skin is typical of that seen in mycosis fungoides and corresponds to the description given by Montgomery. There are a polymorphism of the individual cells and a multiplicity of cell types.

A CASE FOR DIAGNOSIS. Presented by DR. M. H. EBERT and DR. B. B. BEESON.

This woman, aged 56, a native of Moravia, presents a tumor of the left index finger which, she states, was first noted two years ago. There is no history of preceding trauma. The lesion has caused little discomfort, and when pricked with a needle accidentally at any time it did not bleed more copiously than the normal skin. The patient's general health has been excellent, and her family history is irrelevant.

There is a tumor with a broad base on the pulp of the index finger; the growth is cherry-sized, bluish-black, hemispheric and covered with a hard pellicle. The mass of the tumor seems slightly fluctuant in some areas and firm in others. The base is dull red and fairly firm. A bean-sized hard nodule was found in the corium on the posterior surface of the left thigh. The skin over this nodule was brownish red. This tumor was excised for microscopic examination. A similar nodule was found on the right side, and a few varices were present on both legs.

DISCUSSION

DR. A. W. STILLIANS: Clinically I should make a diagnosis of melanoma. I could not discover any significant histologic features by a brief examination.

DR. CLARK W. FINNERUD: I think that the lesion of the finger is suggestive of melanosarcoma and that probably the two lesions on the thighs are not related to it. I saw the section of the lesion which was excised. It is a little hard to classify, but it seems to be an angiofibroma type of lesion, probably a hard fibroma which in places is a little more vascular than these tumors usually are.

DR. WILLIAM ALLEN PUSEY: I got the impression that the lesions on the legs were little tumors of connective tissue.

DR. F. E. SENEAR: I do not wish to make a diagnosis, but I offer a suggestion regarding the lesion on the finger. Recently I saw in the *Annales de dermatologie et de syphilographie* an article regarding myeloplax tumors of the tendon sheaths, which do not often invade the skin but have a tendency to be attached to the tendon sheaths. In an article in the *British Journal of Surgery* is shown a picture of one lesion which invaded the skin and presented a deep bluish color. While I do not venture to make a diagnosis I think that these facts should be taken into consideration. Orthopedists have described these myeloplax tumors frequently and many articles have been written about these growths, but there is a complete lack of accord regarding them. Some authors think that they are sarcomas, and some consider them benign tumors; others regard them as granulomas or reticulo-endotheliomas. There is no agreement even as to the elements that compose them.

DR. M. H. EBERT: In the first place, I realize that the proper place to take a specimen for biopsy is from the tumor itself, but this woman has been frightened and has not reached the psychologic stage in which she will permit this, but she did permit removal of one of the other lesions. The lesion on the finger has been growing steadily for two years, and there is no history of pigmentation in any other part of the body. The reason I mentioned that she was born in Moravia was because it occurred to me that her condition might be a form of Kaposi's sarcoma. It is known that that disorder occurs most frequently in Italy, Czecho-Slovakia, Austria and southern Russia, and this might be significant. I hoped that the small tumor which was excised might be of assistance in the diagnosis. I still believe that the patient has an unusual type of tumor. The cells when studied under oil immersion do not have the appearance of ordinary fibroblasts. I thought that they belonged to the reticulocyte group. The tumor on the finger may show fibrosarcoma or Kaposi's sarcoma. I hope to get a section, and I shall report later.

DR. F. E. SENEAR: I meant to speak about the lesion on the right thigh which is still present. I feel that clinically it is much like fibroma durum or lenticulare. There has been considerable observation recently to show that these tumors are made up of reticulo-endothelial tissue, and it is interesting to find, in view of Dr. Ebert's remark, that this woman may have two types of reticulo-endothelioma.

DR. CLARK W. FINNERUD: The possibility that the lesion on the thigh was of fibroma durum type was discussed. Several tumors of that type have been excised in the last few years, but the histologic picture of these lesions seems to be somewhat different from that in any of the tumors my co-workers and I have examined.

INFECTION OF THE SCALP DUE TO MICROSPORON; PSORIASIFORM LESIONS OF THE FACE, NECK AND HANDS. Presented by DR. JAMES H. MITCHELL and DR. RUBEN NOMLAND.

This boy, aged 3½ years, was first seen by Dr. Nomland at the Central Free Dispensary on Nov. 17, 1934. Both the mother and the child had impetiginous lesions at that time, but the mother's skin has since completely cleared. The lesions developed three days after the child's father brought home a stray, undernourished cat. It is stated that a neighbor child has had similar lesions on the face; that child had a mangy dog with which she had played.

DISCUSSION

DR. M. H. EBERT: What species of Microsporon was found?

DR. JAMES H. MITCHELL: The organism found is either Microsporum felineum or Microsporon lanosum. M. felineum has multitudinous spindles, and the organism found has a few spindles. The rapidity of growth suggests M. lanosum. That organism is found on dogs. The mother today brought some dog's hairs which we shall examine.

TUBERCULOSIS (CUTANEOUS). Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This man, aged 52, states that about three years ago a painless swelling of the thyroid region developed; this ulcerated and drained for two and a half years. One year ago the right axillary glands became swollen, and they have drained at intervals since that time. About six months ago a slightly painful swelling of the left supraclavicular area developed, and later a similar swelling of the left scapular area appeared. The scapular lesion began to exude a thick, yellowish discharge, and the size of the anterior lesions decreased. About one month ago both supraclavicular lesions became ulcerated. These two ulcerated lesions were about the size of a silver dollar; they showed marked undermining of the edges, and a communication became established between the two lesions.

The general health of the patient has been good, except for the fact that he has lost about 15 pounds (6.8 Kg.). There are no cardiorespiratory symptoms. Roentgen examination of the chest showed no abnormalities. The Wassermann reaction of the blood was negative. Blood counts gave essentially normal results.

Histologic examination of a biopsy specimen showed the floor to be composed of infected granulation tissue. The blood vessels showed thickened intima, with marked perivascular round cell infiltration. Here and there a multinucleated giant cell and epithelioid cell could be seen. The histologic picture resembled that of tuberculosis.

DISCUSSION

DR. F. E. SENEAR: I see no particular reason to disagree with the diagnosis as presented. I think that the formation of the bridges, with the development of cribriform ulcers, and the bluish infiltration of the skin extending for considerable distances beyond the ulcers are consistent with the picture of scrofuloderma, and I think that the case can be classed as one of tuberculosis colliquativa.

DR. M. H. EBERT: Was the Wassermann test negative, and has a therapeutic test been made? I ask because at the Central Free Dispensary I have seen two patients with ulcers on the side of the neck that were suggestive of scrofuloderma or tuberculosis colliquativa. These patients' disease proved to be syphilis, and it responded rapidly to therapeutic tests. If the therapeutic test has been made I should say that this is undoubtedly a case of tuberculosis colliquativa.

DR. MAX S. WIEN: The patient has undergone a therapeutic test for syphilis and no improvement has resulted.

A CASE FOR DIAGNOSIS. Presented by DR. F. E. SENEAR and DR. MARCUS R. CARO.

This Negro, aged 26, states that he had syphilis for about five years, for which he received treatment intermittently. The Wassermann reaction of the blood was negative.

An eruption has been present for three or four years, but it has not caused any symptoms and there has been no appreciable extension. The eruption consists of discrete round or oval papular lesions, varying from the size of a pinhead to that of a pea, of the same color as the skin or lighter. These papules are flat-topped or slightly domed, firm and not covered by a scale. They are follicular and are set right in the skin. The eruption involves chiefly the trunk and arms, being most profuse on the sides.

Histologic examination of a biopsy specimen taken from the left flank showed a subepidermal papule about a hair follicle. The overlying epidermis was slightly flattened. There was a thin layer of cellular corium below this, separating it from a fairly well circumscribed papule composed of parallel, horizontally placed, interbranching, densely packed, thickened fibers. These fibers stained well with the Van Gieson stain, showing that they were collagenous. The Weigert stain showed a complete absence of elastic fibers within the papule and fragmentation of fibers in the surrounding corium.

DISCUSSION

Dr. S. W. Becker: Clinically many of these lesions show a follicular orifice in the center, somewhat similar to that which occurs in a certain type of adenoma sebaceum, but the lesions do not have the irregular outline seen in that disorder. Histologically, the section that is presented shows the perifollicular arrangement of the process beautifully and consists of fibrosis of the type seen in cases of scrofuloderma. I have no definite diagnosis to offer.

Dr. M. H. Ebert: The presence of the small amount of atrophy of the shoulders makes me think that the lesions may be small keloids. This man had a keloidal tendency, and it may be that after some transient eruption these keloids formed at the sites of the lesions. I think the histologic picture fits in with that diagnosis.

Dr. William Allen Pusey: That was my impression of the case, that the eruption consisted essentially of perifollicular keloids or scars, if one wants to make the distinction. On the back of the head at the hair line there is a striking resemblance to keloid. I think that some one has described cases of this sort. The lesions are fibrotic, and I think the picture is entirely consistent with the suggestion Dr. Ebert made, namely, that the condition is an acne keloid run wild.

Dr. Marcus R. Caro: It has been my impression that in keloid there is usually less interbranching of collagen fibers than is present in this case. The survival of the hair follicle within the papule also contraindicates the diagnosis of keloid.

Dr. William Allen Pusey: I do not know how a scleroderma could be so sharply confined to perifollicular nodules. So far as I could see, the lesions stood up as white, sharp nodules, and that picture of scleroderma is not familiar to me.

Dr. Clark W. Finnerud: I think, in spite of the difference Dr. Caro spoke of and in spite of the fact that the connective tissue fibers are poor in nuclei, that the diagnosis of keloid is quite logical, and I am inclined to favor it.

Dr. F. E. Senear: We thought neither of keloid nor of scleroderma, and we have no idea what the diagnosis is, but a number of lesions over the lower portion of the trunk appeared to me as being definitely of the soft type, which is seen in the multiple benign new growths of the Schweninger-Buzzi type. I am not able to convince myself that the clinical picture can fit in with the diagnosis of keloid.

Multiple Benign Cystic Epithelioma. Presented by Dr. M. H. Ebert.

This Mexican, aged 26, presents on the face and in and behind the ears an eruption made up of numerous, closely set, hemispheric, firm tumors from the size of a pinhead to that of a pea. Some of these lesions are of the color of the normal skin and others have a slightly translucent appearance. They are crowded closely together in the nasolabial folds, being more discrete on the cheeks and in the ears. The patient states that this trouble began suddenly six weeks ago and that prior to that time his skin was normal. There is no history of a familial occurrence of a similar complaint.

The Wassermann and Kahn reactions of the blood were 2 plus.

Histologic examination of a biopsy from one of the nodules revealed multiple horny cysts. The cell aggregates were of the type seen in basal cell epithelioma and were surrounded by a palisade-like layer. There was little tissue reaction.

DISCUSSION

DR. CLARK W. FINNERUD: This was quite an instructive case clinically. I do not think that any of the members has ever seen a more beautiful microscopic picture of multiple benign cystic epithelioma than the one presented.

DR. S. W. BECKER: This case presents the same picture that I have seen in many slides made from sections of Miss Maude Slye's mice. In many of the mice there develop neoplasms which give a picture identical with the one presented. The tumors in the mice originate from the hair follicles.

DR. M. H. EBERT: I have tried to break down this man's statement that these lesions are of only six weeks' duration. I believe that owing to his poor knowledge of English he may not understand, but he insists that his statement is true. Such an acute onset would be unusual. Moreover, this patient is a man, and I think that most of the cases of multiple benign cystic epithelioma have been reported in females. There is no familial history of similar disease in this case.

CUTANEOUS TUBERCULOSIS. Presented by DR. F. E. SENEAR and DR. HENRY C. SCHORR.

A Negress, aged 22, married, a waitress, states that five months ago she first noticed two nodules on the medial inferior quadrant of each breast. Since then many more similar nodules have appeared in the urogenital region and on the arms, knees, face and eyelids. The patient has no other complaint, except that two weeks ago she had a "cold," and on one occasion she coughed up some blood. There is no history of carcinoma in the family.

The nodules are hard and shotlike, and range in size from that of a small pea to that of a bean. The cervical and epitrochlear glands are enlarged and palpable.

Fluoroscopic and roentgen examination of the chest showed increase in the shadows at the hili and linear markings, especially on the right side. There was no definite parenchymal infiltration. Linear density was noted in the region of the interlobar fissure between the upper and middle lobes of the right lung. These findings were consistent with the diagnosis of old hilar tuberculosis.

Two lesions removed for histologic examination showed a subcutaneous nodule with the histologic picture of tuberculosis, with central caseation and necrosis. No tubercle bacilli were found.

DISCUSSION

DR. RUBEN NOMLAND: I think this patient presents a typical lichenoid type of sarcoid as seen in Negroes. In one of the six cases I reported a short time ago (Nomland, R.: Hematogenous Cutaneous Tuberculosis [Sarcoid] in Negroes; Report of Six Cases, ARCH. DERMAT. & SYPH. **30**:59 [July] 1934) there was marked enlargement of the regional lymph glands. I suggest that the condition be called "hematogenous cutaneous tuberculosis," to qualify it a little.

DR. F. E. SENEAR: The members agree with Dr. Nomland on his point. In line with the discussion of last month (Ebert, M. H.: Tuberculosis Cutis Luposa, ARCH. DERMAT. & SYPH. **31**:748 [May] 1931) in regard to placing these lesions with any degree of accuracy, we chose to call the disease tuberculosis because the histologic picture was definitely that of tuberculosis. It did not show the architecture of sarcoid, but clinically, the lesion could be classed as a sarcoid.

SYPHILIS OF THE PENIS ASSOCIATED WITH LYMPHOGRANULOMA INGUINALE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This Negro, aged 32, presents a lesion of two years' duration on the penis. He states that it began as a painless papule which ulcerated and steadily increased in size. There is edema of the penis of two weeks' duration. In 1927 the patient had bilateral suppurative inguinal adenitis; this healed spontaneously in 1928. There is no known history of a previous genital lesion.

The penile lesion consists of a dollar-sized ulcerating area with a serpiginous border and a friable, hemorrhagic base. Three fistulous openings with puckered fibrous areas about them are present on the foreskin. In both inguinal regions there are scarred areas with puckered bands.

The Frei test was positive, and the Wassermann reaction of the blood, negative. The patient states that since 1933 he has received one hundred and twenty injections in the arm and hip in various clinics throughout the country.

Histologic examination of a biopsy specimen showed that the cutis was composed of granulomatous tissue. The blood vessels showed thickening of the walls, markedly proliferated intima and, in numerous places, obliteration of the lumen. About the vessels was a marked lymphocytic and plasma cell infiltration with many eosinophils.

DISCUSSION

DR. S. J. ZAKON: I believe that the elephantiasis of the penis and the ulcer are the end-results of lymphogranuloma inguinale. The same lesions are observed in women with elephantiasis of the vulva.

DR. M. H. EBERT: I do not believe that from the histologic picture one could make a diagnosis of a gummatous lesion, but I did not have much opportunity to study the specimen. It seems that if the lesion was a gummatous process it would respond to antisyphilitic therapy.

DR. MAX S. WIEN: The presence of an old infection of lymphogranuloma inguinale in this case is evidenced by the old healed inguinal scars of characteristic type and the positive Frei test. We do not feel that the edema of the penis present in this case is comparable to that noted in cases of esthiomene since it has appeared only in the past week, during the antisyphilitic regimen (Herxheimer?), and it lacks the infiltrative tenseness usually noted in the chronic elephantiasic swelling observed in cases of esthiomene.

When this patient was first seen in the clinic we believed that the condition was a malignant degeneration, a nodular ulceration associated with lymphogranuloma inguinale or a gumma.

We have seen five cases of lymphogranuloma inguinale in which superficial ulceration occurred. This type of ulceration may occur as a reaction secondary to a suppurative lesion or be of a primary nature, in which case it simulates granuloma inguinale clinically.

As to the histologic sections, they have been studied carefully with Dr. Jaffé, and he makes a diagnosis of gumma on the section from the nodule on the penis. The appearance today, after the short course of antisyphilitic therapy with mercury and potassium iodide, seems to indicate that there is marked improvement. The patient apparently has gumma of the penis in association with lymphogranuloma inguinale, but the two conditions are not at all related.

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## BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

*Regular Meeting, Dec. 27, 1934*

LOUIS CHARGIN, M.D., *President*

NICKEL DERMATITIS. Presented by DR. LOUIS CHARGIN for DR. FRED E. MAISEL.

G. R., a man, aged 20, single, was first seen in November 1934 at the Mount Sinai Hospital in the clinic for adult patients with allergic conditions. He had a generalized recurrent eruption of about one year's duration.

When the patient was seen in February there were pinhead-size, discrete and confluent papulovesicular purplish-red lesions on the head, neck, upper extremities

and back; a solitary group of vesicular lesions was seen on the glans penis. There were no lesions in the mouth. A biopsy had been performed, and the results were reported as neurodermatitis. Examination of the blood showed eosinophilia.

A relationship of the cutaneous condition to the patient's occupation suggested itself. Three years previously he had begun to work as a salesman of kitchen-ware. After he had worked in that capacity for about two years, the present cutaneous trouble developed. He left his position in June 1934, and within one month his dermatitis began to clear up. By the end of the summer it was practically gone. In the fall he resumed selling kitchen-ware, and in one month the cutaneous lesions again reappeared, though in a milder form.

Specimens of different dyes used in painting the crockery were obtained in dry form, and patch tests were made. These tests proved negative. Tests with excelsior, camphor, carbon-paper and dust from packing cases also proved negative. Patch tests with sterling silver and silver-plated cutlery proved negative, but tests with two pieces from a nickel-plated spoon gave a 3 plus reaction in forty-eight hours. This test was repeated, and the results were confirmed. Control tests on three other patients gave negative results. The alloy used for silver plating contained 18 per cent nickel, 18 per cent zinc and 64 per cent copper.

Tests with a penny, nickel and dime resulted in dirty, brownish-green or copperish discoloration of the skin of the patient as well as of controls. Patch tests with the following substances in dry form were inconclusive because of irritating reactions: powdered copper, powdered tin, cobalt nitrate, ferric sulphate, powdered zinc, cobalt sulphate, cobalt chloride, ferric chloride, cobalt acetate and nickel sulphate.

Tests with various metallic salts in from 1 to 10 per cent solutions were made, and a 1 plus reaction to cobalt nitrate and nickel sulphate in the 10 per cent solution was obtained. Two allergic persons on whom control tests were made also reacted positively, and one control reacted more markedly than this patient to the salts of cobalt and to those of nickel.

Since the patient has been using calamine lotion tests with the ingredients of that drug were made and gave negative results.

DISCUSSION

DR. CHARLES WOLF: I saw this patient when the eruption first appeared, and it suggested pityriasis rosea. Other dermatologists who saw the patient at the same time did not agree with that diagnosis. However, the eruption persisted beyond the usual period, and that diagnosis was dropped. Now a diagnosis of an allergic cutaneous condition seems to be the correct one. It is interesting that in so many cases of this type one cannot discover the particular offending agent in spite of diligent search.

DR. L. SPIEGEL: It would be interesting to ascertain whether this eruption was due to nickel by testing a section of the skin spectrographically.

DR. ADOLPH ROSTENBERG: In regard to Dr. Wolf's remark, I wish to state that I have observed a reaction due to gold sodium thiosulphate which presented the characteristics of pityriasis rosea.

DR. MARION B. SULZBERGER: The question arises as to whether this condition is not an ordinary atopic dermatitis (disseminated neurodermatitis). In cases of dermatitis of that type it is not at all unusual for the patients to show positive reactions to patch tests with nickel salts. No one knows what these positive reactions really mean. They certainly do not necessarily indicate that the dermatosis was caused by the nickel. Steiner (Steiner, K.: *Arch. f. Dermat. u. Syph.* **157**:600, 1929) reported a series of such atopic cases. Practically all the patients (81.25 per cent) gave positive reactions to patch tests with salts of heavy metals; 56.25 per cent were hypersensitive to nickel sulphate. At Dr. MacKee's clinic at the Post-Graduate Medical School and Hospital tests with nickel sulphate were made on many patients with atopic dermatitis, and positive reactions to patch tests with this salt were obtained. My co-workers and I could not make up our minds that this reaction was of any clinical significance. Dr. Gaul at the same clinic has found

that there is an increase in the heavy metal contents of the skin in some of these cases. The heavy metal the content of which is increased is, however, not nickel but copper. We tested our patients with copper salts, but in general they gave negative reactions to tests with these substances. I may add that the patch tests we made were performed with the salts in such concentration (from 1 to 5 per cent) that no reaction was elicited in a large series of normal controls. It is also noteworthy that the reactions to patch tests with nickel salts in atopic dermatoses do not look like the ordinary eczematous responses to patch tests in contact dermatoses. The lesions are more papular and pustular, and sometimes they are follicular. The significance of the reaction is as yet unexplained.

DR. FRED E. MAISEL (by invitation): Except for cases of nickel dermatitis in workers engaged in the nickel-plating process, it seems that until recently cases of dermatitis due to nickel have been infrequently reported. Blaschko in 1889 first described cases of nickel dermatitis in industrial workers; since then other cases have been reported. On closer analysis, however, these cases appear not to be clearcut cases of proved sensitivity to nickel. Other substances, such as lime, petroleum and benzene, are used in nickel-plating and may have played an important part which was overlooked. Lain's report of three cases appears to have been the first mention of localized dermatitis produced by the nickel in spectacle frames. Nickel-plated watches were found to be etiologic factors by Du Bois. Similar cases were reported by Fox, Stewart and Goldman.

A consideration of the theoretical mechanism in this case merits some discussion. The question is: Did the nickel act as a direct chemical irritant? If so, the initial lesions should have developed at the point of contact, namely on the hands. At no time were there lesions on the hands. To explain the widespread generalized dermatitis in this case it is necessary to assume that the nickel was absorbed and that the skin generally became sensitized to it. The mechanism is somewhat akin to that of a dermatitis due to Rhus, except that in dermatitis due to Rhus the initial lesion develops at the site of contact. No atopic bodies have been found, and no efforts at passive transfer have given successful results in either type of dermatitis.

Stewart mentioned the case of an allergic patient on whose skin welts developed at points of contact with objects containing cobalt and nickel and who assumed an inherent sensitivity. He considered an acquired sensitivity one which develops, for example, in industrial workers who come in contact with nickel. It seems that in persons with a marked predisposition to nickel sensitivity, small amounts, for example, such as those contained in cutlery, may cause a reaction. There are no reports concerning the reactions which industrial workers suffering from nickel dermatitis exhibit to the nickel-plated objects or utensils they wear or use at home.

Ordinary silver-plated cutlery has a coating of silver over an alloy containing nickel, but with use this silver coating wears off, thus exposing a surface of nickel-plating. Certainly the common use of nickel ware in the form of kitchen-ware and other objects used in everyday life should make one think more of nickel as a possible cause for many cases of dermatitis.

KERATODERMA BLENNORRHAGICUM. Presented by DR. SAMUEL FELDMAN.

This patient was presented at a meeting of the Society in November 1932 (ARCH. DERM. & SYPH. **27**:889 [May] 1933).

He is presented again because of a recurrence of the symptoms in the joints as well as of the cutaneous lesions. The clinical picture is similar to that which existed when the patient was first shown.

Roentgen examination now reveals atrophic changes in the bones of the left hand, wrist and knees. The blood count shows no abnormalities. Treatment with gonococcus vaccine has again been instituted.

DISCUSSION

DR. ADOLPH ROSTENBERG: It seems to me that such cases occur with greater frequency. This patient shows only two of the characteristic features present in

these cases, namely arthritis and lesions that look like the heaped-up keratotic papules seen in cases of keratoderma blennorrhagicum or in psoriasis arthropathica. I think that the name keratoderma blennorrhagicum is a bad one. The syndrome should be called dermatitis rupioides arthropathica.

DR. THEODORE ROSENTHAL: I agree with Dr. Rostenberg. I do not believe that this patient has keratoderma blennorrhagicum because there is no history of gonorrhea. Not only does he have a heaped-up scaly eruption on the thighs, but he has lesions on the scalp and on the nail of one finger; this shows a definite yellowish discoloration accompanied by a subungual keratosis. I think that this is a case of psoriasis arthropathica.

DR. PAUL GROSS: Keratoderma blennorrhagicum is an etiologic diagnosis, and I cannot conceive of the existence of that condition without a prior or present gonorrheal infection. In this case there is no evidence of gonorrhea. The patient has polyarthritis, and it should be left to the internist and roentgenologist to define the nature of the arthritis. The fact that the cutaneous lesions are so atypical is in favor of the diagnosis of psoriasis arthropathica, and I suggest that careful chemical examination of the blood, particularly of the cholesterol metabolism, be made to see whether the recent findings regarding psoriasis are substantiated in cases of psoriasis arthropathica.

DR. HENRY SILVER: I have repeatedly pointed out that keratoderma blennorrhagicum and psoriasis arthropathica constitute one syndrome with a variant etiologic factor. The clinical and histologic similarity of the two conditions is too great to permit an attempt at differentiation (ARCH. DERMAT. & SYPH. **16**:741, 1927; **27**:889, 1933; **27**:894, 1933).

DR. SAMUEL FELDMAN: I also wonder whether the two conditions are not identical. This patient was in the hospital two years ago, and the case was then studied thoroughly. No gonococci were found, and the complement-fixation test for gonorrhea was negative; yet improvement occurred under treatment with gonococcus vaccine. However, the disease has recurred with renewed vigor each winter since then.

LICHEN PLANUS WITH PALMAR LESIONS. Presented by DR. ARTHUR SAYER.

A. R., a man aged 72, is presented from the clinic of the Mount Sinai Hospital. The eruption began six weeks ago and involves the trunk, the wrists and the glans penis. The lesions are typical lichen planus papules. There is only slight itching.

The unusual feature in this case is the presence of many flat, shiny, polygonal papules on the palms. In color and appearance they are similar to the lesions around the wrists. They appeared at the same time as the lesions on other parts of the body. There is no scaliness and no formation of vesicles.

A biopsy on one of the palmar lesions showed only slight inflammatory changes and few of the characteristic features seen in cases of lichen planus.

EPITHELIOMA ON THE BASIS OF A RADIODERMATITIS. Presented by DR. VAN ALSTYNE H. CORNELL and DR. MAX BERKOVSKY.

M. F., an elevator operator aged 41, is a patient at the Metropolitan Hospital. Twenty-one years ago there developed a sycosis vulgaris, for which he was treated with local medicaments at several clinics. After three months of futile therapy he received roentgen treatment to the face for about nine months, as a result of which a chronic roentgen ray dermatitis developed. About four years ago he noticed a slight erosion on the cheek which gradually became more ulcerated.

There is a chronic roentgen ray dermatitis of the face and neck with characteristic atrophy, scarring and telangiectasia. On the left cheek next to the left naris is a pea-sized ulceration with an elevated, somewhat pearly border. The granulation is clean, and part of the ulcer is covered with a crust. There is a palpable submaxillary gland on the left side.

DISCUSSION

DR. V. A. H. CORNELL: In the treatment of cutaneous diseases by roentgen rays and radium, keratoses most often occur after third degree burns, less often after second degree reactions and occasionally from a single first degree reaction. They may appear after frequent mild erythematous reactions or after months and years of treatment that never caused a reaction. They are most apt to occur on skin which is already telangiectatic or atrophic. They may be warty and keratotic, and sometimes years elapse before they develop. In the beginning they are not epitheliomatous, but they should be regarded as preepitheliomatous changes and treated as such. Ulcers are apt to develop after severe reactions or after reactions that occur over a prolonged period. Sometimes these ulcers heal spontaneously or after mild treatment, or they may persist in spite of all treatment and result in cancerous degeneration. The type of cancer which occurs is generally of the squamous cell variety, but basal cell epitheliomas and sarcoma have been observed. They appear to be rather of a low degree of malignancy, and for this reason as well as because of present sclerosis metastasis is sometimes delayed for many years. The case under consideration is a good example of the condition. The man received roentgen treatment for sycosis vulgaris twenty-one years ago. Nine months later dermatitis developed. The epitheliomatous lesion which is present did not appear until four or five years ago.

ANAPLASTIC EPITHELIOMA OF THE PAROTID GLAND REGION. Presented by DR. WILLIAM HARRIS (by invitation).

F. A., aged 62, presents a mass in the left parotid region. He has had extensive roentgen treatment by a physician.

In the left parotid region there is an ulceration surrounded by a large, hard swelling measuring 8 by 8 cm. The skin is rough and purplish red. Several hard cervical lymph nodes are palpable on the left side of the neck. There is a facial paralysis on the left side.

The result of the pathologic examination was reported as anaplastic epidermoid carcinoma.

PRICKLE CELL EPITHELIOMA OF THE PENIS. Presented by DR. WILLIAM HARRIS.

This man, aged 60, was admitted to the Morrisania City Hospital on Jan. 5, 1932, because of a perineal abscess which was incised and drained. He was in the hospital previously in June 1931, when a circumcision was performed because of an ulcer on the foreskin. This ulcer proved to be a prickle cell epithelioma. A biopsy of the lesion on the penis on the second admission again showed prickle cell epithelioma. There are hard, movable glands in both inguinal regions.

MELANOMA. Presented by DR. WILLIAM HARRIS.

This woman, aged 34, has had a pigmented mole on the right leg since birth. Two weeks before admission she sustained an injury to this mole, and an ulcer formed.

On the outer aspect of the lower part of the right leg is an ulcerated area 5 by 3 cm. The borders are not infiltrated. There are no enlarged inguinal glands. The result of the pathologic examination was reported as melanoma.

On March 24, 1932, radium therapy was given to an area 3.5 by 6 cm., with a 1 mm. platinum filter, the dosage was 1,000 mg. hours. On April 13, 1932, the same dose was repeated. The total dose was 2,000 mg. hours. The dose per square centimeter was 100 mg. hours. On Oct. 5, 1932, the pigmented area in the center of the ulceration was excised. On Sept. 20, 1933, the ulceration was completely healed.

DISCUSSION

DR. WILLIAM HARRIS (by invitation): In the treatment of cutaneous epitheliomas either surgical or radiation therapy or a combination of both may be used. The main object of the treatment must always be the complete eradication of the

lesion. The treatment should not endanger the life of the patient. An attempt to obtain a good cosmetic result should be made, but this aim should always remain secondary. Many patients have lost their lives because of conservative therapy which was inadequate.

A biopsy should be performed whenever possible.

Radiation therapy is the method of choice in the treatment of a large majority of cutaneous malignant lesions. Surgical intervention may be used in cases of lesions around the eyelids, alae nasi and auricles of the ear, especially when there is infiltration of the cartilage. Bulky lesions on the torso and extremities also occasionally lend themselves better to surgical excision. Lesions which fail to respond to radiation therapy are usually best treated by electrosurgery or excision, followed by plastic repair when necessary. Further experience with the Coutard principle of protracted irradiation may extend the use of radiation therapy even to the aforementioned infiltrating epitheliomas.

In planning radiation therapy in cases of cutaneous malignant lesions the complete treatment should be given either in one sitting or in a consecutive series of treatments. Multiple or repeated series of treatments should not be used.

Preliminary curettage or electrosurgery is usually unnecessary except to obtain material for biopsy. On small lesions similar results may be obtained by either roentgen or radium therapy. In small lesions around the eyelids, intrinsic radiation in the form of implantation of filtered radons may be of value. Such implantation is also valuable in cases of glandular metastases.

The secret of success in all types of radiation therapy is a complete knowledge of the subject and the use of an accurately calibrated apparatus. Thorough treatment results in a high incidence of cures. Recurrence after irradiation usually renders the lesion extremely radioresistant.

DR. PAUL GROSS: One feature of basal cell epithelioma should be borne in mind; that is, its potentiality for malignant changes and metastasis to the bony structures, especially to those of the nose and orbit.

I am of the opinion that multiple superficial basal cell epithelioma showing a predilection for the trunk and the histologic picture of multicentric epithelioma is a definite entity. I believe that insufficient proof has been furnished to warrant accepting the position taken by Ayres and Anderson that this type of epithelioma is due to arsenic.

DR. SAMUEL M. PECK: The important thing in the treatment of pigmented tumors is to make a diagnosis first. There is a tendency to call every pigmented growth a melanocarcinoma. Even the pathologist is too prone to make that diagnosis. While one should always bear in mind the tendency of melanocarcinoma to metastasize, radical treatment is not necessary in all instances. Thorough excision well beyond the border of the lesion either with the electric knife or by surgical means gives good results even without radiotherapy. It seems to me that pathologists who specialize in a study of cutaneous diseases and general pathologists are not well acquainted with Bloch's pigmented epithelioma, which is a benign lesion often mistakenly reported on as melanocarcinoma. It is well to remember that a pigmented tumor, no matter what its structure, showing a great many mytotic figures is the type that has a great degree of malignancy, while the amount of pigment is no criterion of the grade of malignancy. A dopa reaction is important only in the diagnosis of amelanotic tumors.

DR. SAMUEL FELDMAN: The various phases of epithelioma have been touched on, and I think it important to raise a few points on the precancerous dermatoses.

According to von Bergmann there is no primary cancer of the skin. All cancers of the skin are preceded by some local pathologic process, which Orth named precancerous dermatosis.

The pathologic changes which one may find in the corium in precancerosis are: degeneration or loss of the elastic tissue, changes in the collagen, increased vascularity and edema and lymphocytic infiltration. The epithelium may be hypertrophied; there may be hyperplasia of cells with hyperchromatosis of the nuclei, hyperkeratosis, and acanthosis, and there may be a fraying of the edges of the epithelium.

Acanthosis is invariably found in all cases of inflammatory and ulcerative types of precancerosis, for example, traumatic ulcerations in the mouth. Cancer may also start in the acanthosis of leukoplakia and in the type of pathologic changes which are found on the edges of tuberculous and syphilitic ulcers.

The degenerations and atrophies of the skin are the precursors of a large number of cutaneous cancers. These dermatoses include senile degeneration, poikiloderma, kraurosis vulvae, "x-ray skin," sailor's skin and similar conditions resulting from overexposure to sunlight and also from congenital diseases such as xeroderma pigmentosum.

One should avoid the use of roentgen rays and radium in the treatment of these maladies, as radiotherapy is capable of producing precisely the condition for which remedy is sought.

Some dermatoses, like senile keratosis, seborrheal warts or arsenical keratosis, are fertile soil for the development of cancer. The presence of lymphocytic infiltration should be regarded as an additional danger signal.

Last, but not least, I must mention an important group of precancerous dermatoses, namely, the benign tumors. Even the common wart may degenerate into a malignant neoplasm, particularly if it is located on a mucous membrane. Among the various blemishes of the skin, lentigo and the nevi bear watching. Nevi in which the pathologic process is located at the junction of the epidermis and the cutis are the ones which may ultimately end in melanoma.

I do not agree with those who advocate leaving these growths untreated. On the contrary, wide excision with the endothermy knife will remove a constant source of danger to the patient.

DR. MARION B. SULZBERGER: In recent years the condition described as erythroplasia of Queyrat has been encountered. Although neither clinical nor microscopic examination suggests the presence of malignant changes, observation and experience have proved that the lesion of that disease inevitably gives rise to cancer, usually of the prickle cell type (sometimes the picture is similar to that observed in Bowen's disease). Erythroplasia is therefore not cancer, but it invariably becomes cancer; it is then a true precancerosis, by definition.

The treatment is that of cancer, that is, complete destruction by means of the usual methods used in treating cancers of similar extent and located in the same areas (ARCH. DERMAT. & SYPH. **26**:1124, 1932; **27**:688, 1933; **28**:798, 1933).

DR. DAVID L. SATENSTEIN: Basal cell epithelioma remains basal cell and never changes into prickle cell; that is definite. I can confirm Dr. Wolf's statement that basal cell epithelioma may be malignant since six such cases have been observed at the Post-Graduate Medical School and Hospital. In considering epithelial tumors it is not as much the type of cell that is important as what the cell is doing. A further point which I should like to stress is that in cases in which treatment with radium or roentgen radiation has resulted in so-called cure a microscopic examination may show that the cure has not been complete.

I have never seen an epithelioma develop in a nevus situated in the cutis. I have seen some nevi that develop in the epidermis become prickle cell epithelioma. There is still another type of epidermal nevus, i. e., the pigmented nevus. In such nevi the amount of pigment has nothing to do with the tendency to malignant degeneration.

With regard to so-called melanoma, a few years ago there appeared a report on a series of two hundred and fifty cases in which treatment was applied and cure resulted. It is most likely that the author was not dealing with melanoma but rather with pigmented lesions.

DR. ISADORE ROSEN: In adhering to more conservative methods of treatment one can avoid the dreaded sequelae of radiodermatitis and subsequent epithelioma as demonstrated by Dr. Cornell and Dr. Berkovsky. I have never observed radiodermatitis in patients I treated because I do not use roentgen rays indiscriminately. I advise against the use of roentgen rays in such diseases as psoriasis, sycosis, lupus erythematosus, hypertrichosis, etc. It is also important to remember that

patients often state that they have not received roentgen treatment before; in such cases further roentgen irradiation may cause damage.

Dr. Feldman brought out some important facts in his discussion of precancerous dermatoses. I have seen a number of cases of tertiary syphilis of the mouth and leukoplakia in which epithelioma developed after treatment with arsenical preparations. I have often emphasized this, a point with which others, especially older clinicians, do not agree.

I agree with Dr. Harris that in the treatment of prickle cell epithelioma it is important to attack the lesions properly or not at all. It is true, however, that in some cases the lesions recur no matter how thorough the therapy may be.

DR. ADOLPH ROSTENBERG: Basal cell epithelioma should and can be treated by every dermatologist who possesses a modern roentgen equipment and a diathermy outfit.

I fully agree that biopsies are essential, but one should not set aside one's clinical experience. Moreover, not all are so fortunate as to be able to obtain the services of a competent histopathologist. The diagnosis made by the average hospital pathologist is, in my experience, of limited value.

What is a precancerous dermatosis? The late Dr. Highman emphatically rejected this term and said that either a lesion is a cancer or it is not. He thought it dangerous to speculate regarding the final outcome. I did not agree with him. I believe that certain cutaneous lesions, such as senile warts, the lesions of Bowen's disease and a few others, should be destroyed as soon as they are recognized. In my opinion Paget's disease is the most important disease of this group, and it should be treated with radical surgical measures once the diagnosis is established.

# Directory of Dermatologic Societies *

## INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.
Place: Budapest, Hungary. Time: Sept. 15-21, 1935.

## FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)
H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.
Place: Toronto, Ont. Time: May 1936.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY
Henry MacCormac, President, 23, Wimpole St., London, W. 1.
R. T. Brain, Secretary, 132, Harley St., London, W. 1.

## NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY
Harry R. Foerster, Chairman, 208 E. Wisconsin Ave., Milwaukee.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Kansas City, Mo. Time: 1936.

AMERICAN DERMATOLOGICAL ASSOCIATION
Charles M. Williams, President, 114 E. 54th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

## SECTIONAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY
Joseph E. Gately, President, 1129 Calvert St., Baltimore.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY
John R. Schermerhorn, President, 1225 Union St., Schenectady.
L. de Mello, Secretary-Treasurer, Medical Arts Bldg., Syracuse.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION
Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: 1935.

IOWA AND WESTERN ILLINOIS DERMATOLOGICAL ASSOCIATION
J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.
Place: Iowa City. Time: Oct. 15, 1935.

NEW ENGLAND DERMATOLOGICAL SOCIETY
William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY
J. W. Roussel, Chairman, 150 Baronne St., New Orleans.
Cornelius F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

## STATE DERMATOLOGIC SOCIETIES

### California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Ernest K. Stratton, Chairman, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

### Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
J. J. Saxton, Secretary, 205 Zack St., Tampa.

### Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

### Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. MacKee, Chairman, 200 W. 59th St., New York.
Lopo de Mello, Secretary, Medical Arts Bldg., Syracuse.

### Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

### Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

### Minnesota Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

### Oklahoma State Dermatological Society

C. L. Brundage, President, 1200 N. Walker St., Oklahoma City.
M. M. Wickham, Secretary, 716 W. Symmes St., Norman.

### Texas Dermatological Society

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

## LOCAL DERMATOLOGIC SOCIETIES

### Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

### Bronx Dermatological Society

Eugene F. Kelley, Chairman, 93 Radford St., Yonkers, N. Y.
Henry Silver, Secretary, 290 West End Ave., New York.

### Brooklyn Dermatological Society

Jacob Skeer, President, 272 E. 19th St., Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Albert R. McFarland, President, 315 Alexander St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CHICAGO DERMATOLOGICAL SOCIETY

William A. Pusey, President, 7 W. Madison St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

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Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

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E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

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William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

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Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

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Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

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Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

PITTSBURGH DERMATOLOGICAL SOCIETY

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J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

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